

An addendum to this minute has been included at the end of the document.

**6.15 BEVACIZUMAB,
Solution for I.V. infusion, 100 mg in 4 mL and 400 mg
in 16 mL
Mvasi[®],
Amgen Australia Pty Ltd**

1 Purpose of Application

- 1.1 The minor submission requested changes to the restriction wording for bevacizumab for the treatment of non-small cell lung cancer (NSCLC) under Section 100 (Efficient Funding of Chemotherapy) so that it aligns with the TGA-approved indication for the biosimilar brand of bevacizumab (Mvasi[®]), hereafter referred to as Mvasi.

2 Background

Registration status

- 2.1 Mvasi was TGA approved as a biosimilar with the same indications to the reference brand Avastin and was registered on the ARTG on 30 June 2020.
- 2.2 Bevacizumab is TGA approved for use in combination with carboplatin and paclitaxel for first-line treatment of patients with unresectable advanced, metastatic or recurrent, non-squamous NSCLC (draft Product Information (PI)). Bevacizumab is not specifically registered for use in combination with atezolizumab for NSCLC.
- 2.3 Atezolizumab (Tecentriq[®]) is TGA approved for the following indications for NSCLC (atezolizumab PI, p1):
- a. in combination with bevacizumab, paclitaxel and carboplatin, for the first-line treatment of adult patients with metastatic non-squamous non-small cell lung cancer (NSCLC). In patients with EGFR mutant or ALK-positive NSCLC, in combination with bevacizumab, paclitaxel and carboplatin, only after failure of appropriate targeted therapies.
 - b. in combination with nanoparticle albumin-bound paclitaxel (nab-paclitaxel) and carboplatin, for first-line treatment of patients with metastatic non-squamous NSCLC who do not have tumour EGFR or ALK genomic aberrations.
 - c. as monotherapy for the treatment of adult patients with locally advanced or metastatic NSCLC after prior chemotherapy. Patients with EGFR mutant or ALK-positive NSCLC should also have received targeted therapies before receiving Tecentriq.

Previous PBAC consideration

- 2.4 At the November 2020 meeting, the PBAC recommended listing Mvasi, under Section 100 (Efficient Funding of Chemotherapy) for all of the indications for which the reference brand, Avastin is currently PBS-listed. The PBAC recommended listing Mvasi on a cost-minimisation basis to the Avastin brand of bevacizumab, and noted that this would result in no net cost to the Government because the listing of Mvasi is not expected to grow the market.
- 2.5 At the March 2019 meeting, the PBAC recommended listing atezolizumab and bevacizumab in addition to platinum-doublet chemotherapy (PDC), for treatment of metastatic non-squamous NSCLC (paragraph 7.2, Atezolizumab and bevacizumab, Public Summary Document (PSD), March 2019). The PBAC considered that there was a high clinical need for new treatment options for that specific patient group (EGFR mutant/ALK positive subgroup post TKI therapy population).
- 2.6 At the March 2011 meeting, the PBAC did not recommend the listing of bevacizumab for (1) initial treatment, in combination with carboplatin and paclitaxel, of a patient with advanced or metastatic non-squamous NSCLC who meet certain criteria and (2) continuing treatment, as monotherapy, in a patient who does not have progressive disease. The PBAC rejected the submission on the basis of an unacceptably high and uncertain cost-effectiveness ratio (bevacizumab PSD, March 2011).
- 2.7 At the time of evaluating the minor submission, Avastin was the only brand of bevacizumab listed on the PBS. Another bevacizumab biosimilar, (Zirabev[®], hereafter referred to as Zirabev), was recommended by the PBAC at its July 2020 meeting with the same PBS listing as Mvasi.

For more detail on the PBAC's view, see section 5 PBAC outcome.

3 Requested listing

- 3.1 The submission requested to remove the requirement that bevacizumab be used in combination with atezolizumab in the bevacizumab restriction for NSCLC. The submission claimed that removing the combination use of bevacizumab with atezolizumab from the PBS listing would allow medical practitioners and patients more choice for treatments of metastatic NSCLC and wider access to biosimilar drugs at lower costs.
- 3.2 Under Initial Treatment 1 of the bevacizumab listing, the requested restriction change would allow for bevacizumab to be used in combination with PDC in patients who have not previously received treatment for their metastatic disease. This population was consistent with that requested in the Avastin submission considered at the March 2011 meeting which was not recommended by PBAC (refer to paragraph 2.6 above). Combination use of atezolizumab in combination with bevacizumab in NSCLC (and hepatocellular carcinoma (HCC)) is provided for by the atezolizumab registration on the ARTG.

- 3.3 Under Initial Treatment 2 of the bevacizumab listing, the requested restriction change would allow for bevacizumab to be combination with PDC in non-squamous type NSCLC and requires the patient to have progressed with a TKI or ALK TKI. This listing would not be consistent with the TGA approved indication for bevacizumab for NSCLC.
- 3.4 The pre-PBAC response clarified the intent of the submission was to address the sponsor's perception of a misalignment between the registration and current PBS restriction of bevacizumab for NSCLC. The pre-PBAC response noted the registration of atezolizumab has been changed to reflect this combination use, however, the registration of the bevacizumab reference brand, Avastin, and biosimilar brands has not been changed. The pre-PBAC response further explained that updating the restriction as requested would not impact on the utilisation of bevacizumab, as quadruple therapy (atezolizumab + bevacizumab + PDC) is currently standard of care in clinical practice.
- 3.5 The PBAC noted that the bevacizumab PI had also not been updated for its combination use with atezolizumab for HCC, which was recommended at the July 2020 PBAC meeting. The PBAC considered that this type of misalignment is likely to be repeated, noting that there are more medicines coming forward for combination use where TGA registration occurs only for the medicines whose patent has not expired. The PBAC considered that changing the current bevacizumab PBS restriction to unrestricted would allow access to combination treatment with atezolizumab. However, the PBAC noted that this would likely increase utilisation by 10-20% (see paragraph 4.5 for further details).

For more detail on the PBAC's view, see section 5 PBAC outcome.

4 Clinical evidence

Sponsor hearing

- 4.1 There was no hearing for this item.

Consumer comments

- 4.2 The PBAC noted and welcomed the input from an organisation (1) via the Consumer Comments facility on the PBS website. Comments from Lung Foundation Australia supported broadening the restriction wording of bevacizumab for NSCLC as it would allow clinicians with flexibility to treat a broader range of patients and providing greater access to biosimilar products. The organisation reiterated its support of subsidising the use of biosimilars from its comments from the November 2020 consideration including wider access to an additional choice of therapy, improvement in patient wellbeing and survivability because of wider access treatment for a broad range of cancers and ensuring continuity of supply and reducing costs of the healthcare system.

Clinical evidence

- 4.3 The minor submission did not provide clinical evidence to support the change of restriction wording.

Estimated PBS usage & financial implications

- 4.4 The minor submission claimed that the amended restriction is not anticipated to change bevacizumab use. However, noting the financial uncertainty arising from the restriction change, the Sponsor proposed a █% price reduction to the price of bevacizumab, in addition to the 25% F2 Statutory Price Reduction, when the NSCLC listing change comes into effect and assumed this would flow on to all bevacizumab brands.
- 4.5 The PBAC considered that changing the current bevacizumab restriction to unrestricted would likely increase utilisation. Noting that only around half of the Stage III ovarian cancer population receive therapy with bevacizumab under current restriction criteria, this use would likely expand to treatment for relapsed disease. The PBAC also noted that there is potential for increased use in glioblastoma, and in non-PBS-reimbursed indications such as non-driver-mutant NSCLC, breast cancer and non-colorectal gastrointestinal cancers in combination with chemotherapy; however, considered that these were not likely to drive significant overall changes in utilisation. The PBAC considered the increase in utilisation would likely be between 10-20% and would result in a net financial cost to the Government. The PBAC considered that it would be reasonable to consider that the use of bevacizumab will expand to the total estimated prevalence of Stage III and IV ovarian cancer in Australia.
- 4.6 As a minor submission, the financial estimates have not been independently evaluated.

For more detail on the PBAC's view, see section 5 PBAC outcome.

5 PBAC Outcome

- 5.1 The PBAC recommended the listing of bevacizumab under Section 100 (Efficient Funding of Chemotherapy) as an unrestricted benefit.
- 5.2 The PBAC noted that for combination cancer medicines, the TGA indications for the newer medicine are updated, while the indications for the older, off-patent medicine, are often not updated. Responsibility for regulatory post-marketing surveillance and conditions-of-approval rests with the sponsor of the newer medicine. This has occurred for NSCLC (before the marketing approval of bevacizumab biosimilars) and also for HCC, and is likely to be repeated for other combinations of newer medicines with bevacizumab.
- 5.3 The PBAC further noted that it would be appropriate to seek a listing for the first biosimilar for bevacizumab that would assure supply across all listed populations. The PBAC noted the supply assurance arrangements that exist under the *National Health Act 1953* and which always apply to the first new brand of a medicine once the medicine becomes subject to the first new brand statutory price reduction and moves

into price disclosure. The PBAC noted that it was common for originator sponsors to cease supply or divest their brands once these mechanisms apply.

- 5.4 The PBAC considered that changing the bevacizumab restriction for all currently listed indications to unrestricted would allow access to combination treatment with atezolizumab so that no patients would be disadvantaged should there be any future concerns around supply of the originator brand. This includes the only currently non-streamlined indication, glioblastoma, changing from a written only authority to an unrestricted benefit. The PBAC considered a maximum amount of 1800 mg and a maximum of 7 repeats would be appropriate for an unrestricted benefit listing.
- 5.5 The PBAC noted that an unrestricted listing for bevacizumab would likely increase utilisation. Noting that only around half of the Stage III ovarian cancer population currently receive therapy with bevacizumab under current restriction criteria, this use would likely expand to treatment for relapsed disease. The PBAC also noted that there is potential for increased use in glioblastoma, and in non-PBS-reimbursed indications such as non-driver-mutant NSCLC and breast cancer and non-colorectal gastrointestinal cancers in combination with chemotherapy; however, considered that these were not likely to drive significant overall changes in utilisation. The PBAC considered this would increase bevacizumab utilisation by approximately 10-20%. The PBAC considered that it would be reasonable to consider that the use of bevacizumab will expand to the total estimated prevalence of Stage III and IV ovarian cancer in Australia. The PBAC noted that it would be reasonable to use the current average treatment course for ovarian cancer as a proxy for all bevacizumab treatment courses, as it noted that actual length of treatment course with bevacizumab on the PBS for the treatment of ovarian cancer has been shorter than was originally anticipated, and so this represented the actual treatment experience in Australia.
- 5.6 The PBAC considered that for this change to be cost-effective, a further 10-20% price reduction would need to be applied to any biosimilar brand of bevacizumab to offset the likely increase in utilisation. This would be in addition to the 25% Statutory Price Reduction when any of the recommended biosimilar brands of bevacizumab is listed on the PBS, as the 25% reduction is not intended to offset the cost of increased utilisation.
- 5.7 The PBAC maintained its view from November 2020 that because Mvasi is not expected to provide substantial and clinically relevant improvement in efficacy, or reduction of toxicity over Avastin, or not expected to address a high and urgent unmet clinical need given the presence of an alternative therapy, the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2009* for Pricing Pathway A were not met.
- 5.8 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

6 Recommended listing

6.1 Amend existing listings for bevacizumab (11727F 11731K 11791N 11811P 10120P 10114H 7243F 10885X 11749J 11745E 10121Q, 10115J, 10881Q, 11803F, 11809M, 4400N, 12166H, 12165G) to one consolidated listing as follows:

6.2 Apply ‘Supply only’ arrangements to all current listings that have repeats listed, upon creation of the above unrestricted benefit.

MEDICINAL PRODUCT Form	PBS item code	Max. Amount	No. of Rpts
BEVACIZUMAB Injection	NEW (Private) NEW (Public)	1800 mg	7
		Max Qty. multiplier: unlimited Repeat increases multiplier: 2	
Available brands			
Avastin (bevacizumab 400 mg/16 mL injection, 16 mL vial)			
Avastin (bevacizumab 100 mg/4 mL injection, 4 mL vial)			
Mvasi (bevacizumab 400 mg/16 mL injection, 16 mL vial)			
Mvasi (bevacizumab 100 mg/4 mL injection, 4 mL vial)			
Zirabev (bevacizumab 400 mg/16 mL injection, 4 mL vial)			
Zirabev (bevacizumab 100 mg/4 mL injection, 4 mL vial)			
Category / Program: Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals			
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners			
Restriction type: <input checked="" type="checkbox"/> Unrestricted benefit			
7608	Administrative advice: Special Pricing Arrangements apply		

This restriction may be subject to further review. Should there be any changes made to the restriction the Sponsor will be informed.

Addendum to the March 2021 PBAC Minutes:

7 Background

- 7.1 Subsequent to the meeting, the sponsor presented a pricing proposal for bevacizumab (Mvasi), offering prices of: \$ [REDACTED] per 100 mg in 4 mL vial; and \$ [REDACTED] per 400 mg in 16 mL vial. The percentage reduction proposed is lower than the 10-20% advised by PBAC, however still incorporates a further reduction above the 25% Statutory Price Reduction that would apply when any of the recommended biosimilar brands of bevacizumab is listed on the PBS.
- 7.2 Current PBS utilisation of bevacizumab in ovarian cancer was reviewed and the Department's modelling indicated that the sponsor's proposed price reduction appears to account for the potential increase in PBS utilisation of bevacizumab in Stage III and IV ovarian cancer.

8 PBAC Outcome

- 8.1 Following review of current PBS utilisation of bevacizumab in ovarian cancer, the PBAC considered that the sponsor's proposed price reduction was reasonable and met the Committee's original intent of offsetting the likely increase in utilisation in Stage III and IV ovarian cancer due to an unrestricted listing.
- 8.2 The PBAC considered it would be informative to review the impact of an unrestricted listing after 12 and 24 months of implementation.
- 8.3 The PBAC reiterated that it would be appropriate to seek a listing for the first biosimilar for bevacizumab that would assure supply across all listed populations and advised the Department to work with the sponsor to ensure suitable arrangements to ensure this were in place.

9 Context for Decision

The PBAC helps decide whether and, if so, how medicines should be subsidised through the Pharmaceutical Benefits Scheme (PBS) in Australia. It considers applications regarding the listing of medicines on the PBS and provides advice about other matters relating to the operation of the PBS in this context. A PBAC decision in relation to PBS listings does not necessarily represent a final PBAC view about the merits of the medicine or the circumstances in which it should be made available through the PBS. The PBAC welcomes applications containing new information at any time.

10 Sponsor's Comment

Amgen welcomes the PBAC's positive recommendation of Mvasi that will enable unrestricted access to bevacizumab for Australian patients. Mvasi provides the same

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health outcomes and is as safe and effective as the reference brand.¹ Biosimilars provide the opportunity for savings to the PBS that will further enable patient access to innovative medicines.

1. Australian Government Department of Health. Biosimilars Awareness Initiative. Biosimilar bevacizumab – fact sheet for consumers and healthcare professionals.
<https://www1.health.gov.au/internet/main/publishing.nsf/Content/biosimilar-awareness-initiative>.
Sourced: 28 May 2021.