

**5.21 BEVACIZUMAB,
Solution for I.V. infusion 100 mg in 4 mL,
Solution for I.V. infusion 400 mg in 16 mL,
Vegzelma[®],
Celltrion Healthcare Australia Pty Ltd**

1 Purpose of Submission

- 1.1 The Category 3 submission requested a Section 100 Efficient Funding of Chemotherapy Program (EFC), Unrestricted Benefit listing of a new biosimilar brand of bevacizumab solution for I.V. infusion 100 mg in 4 mL and 400 mg in 16 mL (hereafter referred to as Vegzelma[®]) under the same circumstances and at the same price as the PBS-listed biosimilar brands of bevacizumab (Abevmy[®], Bevaciptin[®], Mvasi[®]) and to be treated as equivalent for the purpose of substitution.

2 Background

- 2.1 Abevmy, Bevaciptin and Mvasi are currently listed on the PBS as Section 100 EFC, Unrestricted Benefit listings.
- 2.2 Avastin, the reference brand, was delisted at the request of its sponsor, Roche Products Pty Ltd, on 1 June 2021, the same date that the biosimilar brand Mvasi was listed.

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Table 1: Key components of the clinical issue addressed by the submission (as stated in the submission)

Component	Description
Population	Patients with metastatic colorectal cancer, locally recurrent or metastatic breast cancer, advanced, metastatic or recurrent non-squamous Non-Small Cell Lung Cancer, advanced and/or metastatic renal cell cancer, grade IV glioma, epithelial ovarian, fallopian tube or primary peritoneal cancer, recurrent epithelial ovarian, fallopian tube or primary peritoneal cancer and cervical cancer.
Intervention	Vegzelma 100mg in 4mL single dose vial; and Vegzelma 400mg in 16mL single dose vial.
Comparator	Bevacizumab 100mg in 4mL and 400mg in 16mL injections.
Outcomes	<p>Biosimilarity to Avastin.</p> <p>Primary Outcome: Objective Response Rate (ORR) based on the Best Overall Response (BOR) during the Induction Study Period by the Response Evaluation Criteria in Solid Tumours (RECIST) version 1.1.</p> <p>Secondary Outcomes:</p> <ul style="list-style-type: none"> • ORR based on the BOR during the Whole Study Period by the RECIST version 1.1. • Pharmacokinetics: C_{trough} • Quality of life questionnaire scores. • Safety outcomes: incidence and severity of adverse events (AEs), serious AEs (SAEs), treatment-emergent AEs (TEAEs) and immunogenicity.
Clinical claim	Vegzelma is biosimilar Avastin and non-inferior in terms of comparative efficacy and safety. As the currently PBS-listed biosimilars were also compared to Avastin, Vegzelma has been demonstrated to be therapeutically equivalent to these products.

Source: Table 1-1, p13 of the submission.

Registration status

2.3 Vegzelma was Therapeutic Goods Administration (TGA) registered on 5 September 2023 and was determined to be a biosimilar to Avastin. Vegzelma has the same indications as Abevmy, Bevaciptin, Mvasi, that is:

- Metastatic Colorectal Cancer
- Locally recurrent or metastatic Breast Cancer
- Advanced, metastatic or recurrent non-squamous Non-Small Cell Lung Cancer
- Advanced and/or metastatic Renal Cell Cancer
- Grade IV Glioma
- Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer
- Recurrent Epithelial Ovarian, Fallopian Tube or Primary Peritoneal Cancer
- Cervical Cancer

Previous PBAC consideration

2.4 Vegzelma has not been considered by the PBAC previously.

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- 2.5 The biosimilar bevacizumab products, Mvasi, Abevmy and Bevaciptin, were recommended for PBS listing by the PBAC in November 2020, November 2021, and March 2022, respectively. Mvasi, Bevaciptin and Abevmy were listed on the PBS in June 2021, November 2022 and December 2022, respectively.
- 2.6 The bevacizumab biosimilar product, Zirabev[®], was recommended by the PBAC in July 2020. Zirabev has not yet listed on the PBS.

3 Requested listing

- 3.1 The submission requested the listing of Vegzelma under the same conditions as the existing bevacizumab listings. Suggested additions are presented below in italics.

Add brand to existing items:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. amount	No. of Rpts	Available brands
BEVACIZUMAB				
bevacizumab 100 mg/4 mL injection, 4 mL vial	12479T (IP)	1800mg	7	Abevmy Bevaciptin Mvasi <i>Vegzelma</i>
bevacizumab 400 mg/16 mL injection, 16 mL vial				
bevacizumab 100 mg/4 mL injection, 4 mL vial	12508H (IN)	1800mg	7	Abevmy Bevaciptin Mvasi <i>Vegzelma</i>
bevacizumab 400 mg/16 mL injection, 16 mL vial				
Category / Program: S100 – Section 100 (Efficient Funding of Chemotherapy) – Public/Private				
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
Restriction type: <input checked="" type="checkbox"/> Unrestricted				

- 3.2 The submission requested that Vegzelma be treated as equivalent to Mvasi, Bevaciptin and Abevmy for the purpose of substitution. EFC medicines are governed by the *National Health (Efficient Funding of Chemotherapy) Special Arrangement 2011*. Subsection 33(2) of that agreement allows the substitution of brands with the same chemotherapy drug. This means that any PBS listed brand of bevacizumab is already considered equivalent for the purpose of substitution under this arrangement, irrespective of biosimilarity or bioequivalence. Substitution is still at the discretion of the pharmacist and clinical judgement about the suitability of the substitute should still apply.
- 3.3 The submission requested the implementation of biosimilar uptake drivers apply to Vegzelma if listed, however, no uptake drivers can be applied as the requested listing is Unrestricted and Avastin (reference brand) is no longer PBS-listed.

4 Comparator

- 4.1 The submission nominated Avastin as the main comparator. This was appropriate noting that the PBAC recommended listing Mvasi on a cost-minimisation basis to Avastin in November 2020.

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item.

Consumer comments

- 5.2 The PBAC noted and welcomed the input from individuals (1) and organisations (2) via the Consumer Comments facility on the PBS website. The comments described the benefits of having additional treatment options such as Vegzelma on the PBS including flexibility in treatment and potential affordability.
- 5.3 The PBAC noted that the Medical Oncology Group of Australia (MOGA) strongly supported the listing of Vegzelma.

Clinical trials

- 5.4 The submission presented the following clinical trials to support the claim that Vegzelma is similar to Avastin in terms of its pharmacokinetics, efficacy, immunogenicity, and safety. Details of the trials are summarised in Table 2.

Table 2: Trial presented in the submission and associated report presented in the submission

Trial ID	Protocol title/ Publication title	Publication citation
Trial 1 NCT03247673	Phase 1 Randomized, Double-blind, Three-arm, Parallel Group, Single-dose Study to Compare the Pharmacokinetics and Safety of Three Formulations of Bevacizumab (CT-P16, EU-approved Avastin® and US-licensed Avastin®) in Healthy Male Subjects.	03/02/2021 <i>Celltrion 2021</i> ;Version.1: pages1-499
Trial 2	Phase 1, randomized, double-blind, parallel group, single-dose study to compare the PK and safety of CT-P16 and EU-Avastin in healthy Japanese male subjects.	06/10/2021 <i>Celltrion 2021</i> ;Version.1: pages1-140
Trial 3 NCT03676192	A Double-Blind, Randomized, Active-Controlled, Parallel-Group, Phase 3 Study to Compare Efficacy and Safety of CT-P16 and EU-Approved Avastin® as First-Line Treatment for Metastatic or Recurrent non-squamous non-small cell lung cancer	22/02/2022 <i>Celltrion 2022: pages1-218</i>

PK = pharmacokinetics

Source: Table 2-4, p26 of the submission

- 5.5 As a Category 3 submission, no evaluation of the clinical evidence was undertaken.

Clinical claim

- 5.6 The submission noted that the TGA found Vegzelma to be biosimilar to Avastin and that the TGA Delegate considered that Vegzelma had comparable pharmacokinetics, efficacy, safety, and immunogenicity to Avastin.
- 5.7 The submission therefore claimed the non-inferior comparative effectiveness and non-inferior comparative safety of Vegzelma compared with Avastin and other bevacizumab biosimilars by extension.
- 5.8 The PBAC considered that the claim of non-inferior comparative effectiveness and safety was reasonable.

Economic analysis

- 5.9 The submission presented a cost-minimisation analysis of Vegzelma compared with Avastin based on the clinical evidence demonstrating biosimilarity between Vegzelma and Avastin. The equi-effective doses were estimated as 1 mg Vegzelma and 1 mg Avastin (and the other PBS-listed brands of bevacizumab).
- 5.10 The submission stated that the proposed listing would not result in additional costs associated with ongoing patient management and monitoring, co-administered treatments, and other related costs.
- 5.11 The submission requested the same approved ex-manufacturer price (AEMP) for Vegzelma as that of the currently PBS-listed bevacizumab brands. A price disclosure reduction of 25.97% is scheduled to apply to the PBS-listed bevacizumab brands on 1 April 2024.
- 5.12 As a Category 3 submission, the economic analysis has not been independently evaluated.

Estimated PBS usage and financial implications

- 5.13 The submission adopted a market share approach to estimate the utilisation and financial impact of listing Vegzelma. The submission assumed that Vegzelma would substitute for the existing use of the other brands of PBS listed bevacizumab on a 1:1 basis. As such, the submission estimated the requested listing of Vegzelma to be cost neutral to the PBS/RPBS.
- 5.14 The submission considered listing Vegzelma on the PBS is not expected to increase the overall use of bevacizumab on the PBS noting the current market is in a mature and stable state. This is appropriate as it is expected that Vegzelma would substitute for the other brands of PBS listed bevacizumab.
- 5.15 Table 3 presents the estimated extent of use, cost of Vegzelma to the PBS/RPBS, and the net financial implications to the PBS/RPBS.
- 5.16 The submission claimed that the estimated net financial impact to the PBS/RPBS over six years for the listing Vegzelma would be nil.

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Table 3: Estimated use and financial implications

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of scripts dispensed	1	1	2	2	2	2
Estimated financial implications of Vegzelma						
Cost to PBS/RPBS less co-payment	3	4	4	5	5	5
Estimated financial implications of other PBS-listed brands of bevacizumab						
Cost to PBS/RPBS less co-payment	6	6	6	6	6	6
Net financial implications						
Net cost to PBS/RPBS	7	7	7	7	7	7

Abbreviations: PBS = Pharmaceutical Benefits Scheme; RPBS = Repatriation Pharmaceutical Benefits Scheme.

Source: submissions financial model spreadsheet

The redacted values correspond to the following ranges

¹ 5,000 to < 10,000

² 10,000 to < 20,000

³ \$10 million to < \$20 million

⁴ \$20 million to < \$30 million

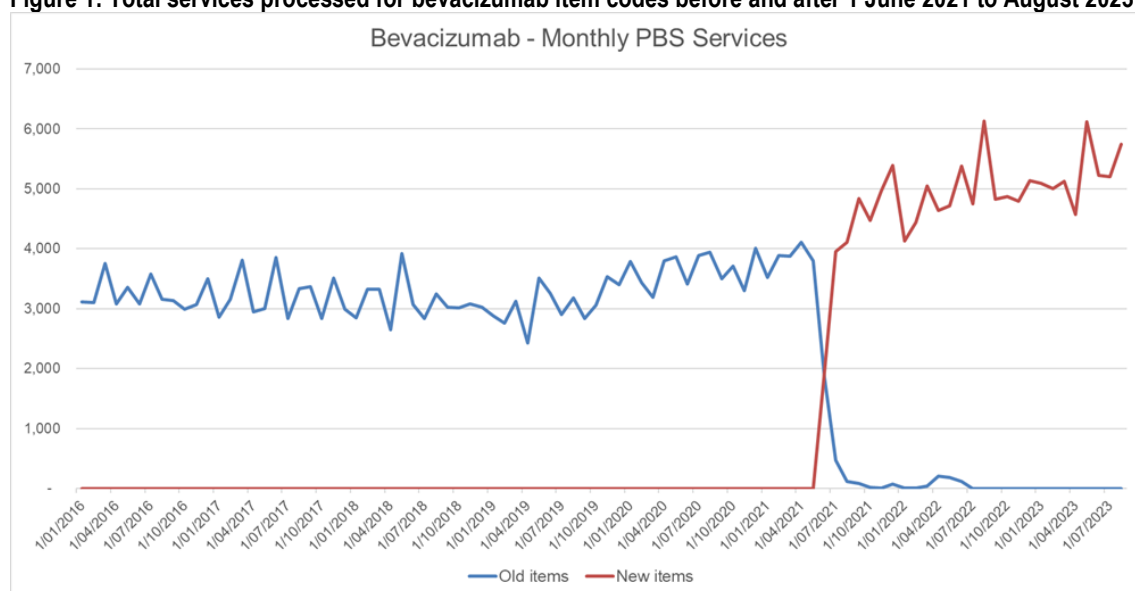
⁵ \$30 million to < \$40 million

⁶ net cost saving

⁷ \$0 to < \$10 million

5.17 The submission presented the number of PBS services processed over the period of June 2021 to August 2023. The utilisation of bevacizumab steadily increased in July 2021 when the new item codes 12479T and 12508H were issued (replacing item codes 10114H and 10115J) (Figure 1).

Figure 1: Total services processed for bevacizumab item codes before and after 1 June 2021 to August 2023



Source: p75, of the submission.

6 PBAC Outcome

- 6.1 The PBAC recommended the Section 100 EFC, Unrestricted Benefit listing of a new biosimilar brand of bevacizumab (Vegzelma) in the forms: solution for I.V. infusion 100 mg in 4 mL; and solution for I.V. infusion 400 mg in 16 mL, under the same circumstances as the PBS-listed biosimilar brands of bevacizumab (Abevmy, Bevaciptin, Mvasi).
- 6.2 The PBAC considered that the nomination of Avastin (the reference brand of bevacizumab) as comparator was appropriate, however, noted that the other biosimilar brands of bevacizumab could also be considered as appropriate comparators.
- 6.3 The PBAC accepted the claim of non-inferior comparative effectiveness and safety of Vegzelma compared to Avastin. This was based on the TGA determination that Vegzelma is biosimilar to Avastin and that the TGA Delegate considered that Vegzelma had comparable pharmacokinetics, efficacy, safety, and immunogenicity to Avastin.
- 6.4 The PBAC considered that it was appropriate for Vegzelma to be cost-minimised to the existing PBS-listed brands of bevacizumab. The PBAC considered that the equi-effective doses were:
 - 1 mg of Vegzelma and 1 mg of Avastin (and of the other PBS-listed brands of bevacizumab).
- 6.5 The PBAC noted that EFC medicines are governed by subsection 33(2) of the *National Health (Efficient Funding of Chemotherapy) Special Arrangement 2011* which allows the substitution of brands with the same chemotherapy drug. The PBAC therefore noted that Vegzelma is to be treated as equivalent to Mvasi, Bevaciptin and Abevmy for the purpose of substitution.
- 6.6 The PBAC noted that the listing of Vegzelma on the PBS was not expected to increase the overall use of bevacizumab on the PBS as it is expected that Vegzelma would substitute for the other brands of PBS listed bevacizumab. The PBAC therefore considered that the estimated net cost to the PBS/RPBS would be nil.
- 6.7 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Vegzelma is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity, over the comparator, and is 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 2022* for Pricing Pathway A were not met.
- 6.8 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

7 Recommended listing

7.1 Add brand to existing items:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Max. amount	No. of Rpts	Available brands
BEVACIZUMAB				
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bevacizumab 400 mg/16 mL injection, 16 mL vial				
Category / Program: S100 – Section 100 (Efficient Funding of Chemotherapy) – Public/Private				
Prescriber type: <input checked="" type="checkbox"/> Medical Practitioners				
Restriction type: <input checked="" type="checkbox"/> Unrestricted				

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

8 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.

9 Sponsor's Comment

The sponsor had no comment.