5.15 BEVACIZUMAB
Solution for I.V. infusion, 100 mg in 4 mL and 400 mg in 16 mL
Zirabev®,
Pfizer Australia Pty Ltd

1 Purpose of Application

1.1 The minor submission requested a Section 100 (Efficient Funding of Chemotherapy) Authority Required (STREAMLINED) listing for a new biosimilar brand of bevacizumab (Zirabev®), hereafter referred to as Zirabev.

2 Background

Registration status

2.1 Zirabev was TGA approved on 21 November 2019 and was determined to be a biosimilar to the reference brand Avastin® (hereafter referred to as Avastin).

2.2 Zirabev was TGA approved for the same indications as the reference brand, Avastin. The TGA considered the extrapolation of indications for Zirabev to all the indications of Avastin in Australia appropriate (TGA Delegate's Overview, p18).

2.3 Zirabev has not previously been considered by the PBAC. Avastin is the only brand of bevacizumab currently listed on the PBS.

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

3 Requested listing

3.1 The submission requested the same listings for all indications for which the reference brand Avastin is currently PBS listed. The proposed dosage, form, strength, maximum quantity and number of repeats for Zirabev are the same as for Avastin:

- Metastatic colorectal cancer
- Advanced, metastatic or recurrent non-squamous non-small cell lung cancer (NSCLC)
- Relapsed or recurrent glioblastoma
- Epithelial ovarian, fallopian tube or primary peritoneal cancer
- Cervical cancer

3.2 The submission requested Authority Required (STREAMLINED) listings for all indications for Zirabev to encourage biosimilar uptake. This is the same type of authority as Avastin for all indications except for relapsed or recurrent glioblastoma,

which is currently a written authority for initial treatment and telephone authority for continuing treatment.

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

4 Consideration of the evidence

Sponsor hearing

4.1 There was no hearing for this item as it was a minor submission.

Consumer comments

4.2 The PBAC noted that no consumer comments were received for this item.

Clinical trials

4.3 The minor submission presented the following clinical trials to support the claim of biosimilarity of Zirabev to the reference brand Avastin. As a minor submission, no evaluation of the clinical evidence was undertaken.

Table 1: Trials and associated reports presented in the submission

Trial ID/First Author	Protocol title/ Publication title	Publication citation
B7391002	A Phase 1, Single-Dose, Single-Arm, Open-Label, Pilot, Pharmacokinetic Variability Study of Bevacizumab Administered Intravenously to Healthy Subjects.	Clinical Study Report Synopsis: Protocol B7391002
B7391001	Phase 1, Double Blind, Randomized, Parallel-Group, Single-Dose, 3-Arm, Comparative Pharmacokinetic Study of PF-06439535 and Bevacizumab Sourced From US and EU Administered to Healthy Male Volunteers.	Clinical Study Report Synopsis: Protocol B7391001.
B7391003	A Phase 3 Randomized, Double-Blind Study of PF-06439535 Plus Paclitaxel-Carboplatin and Bevacizumab Plus Paclitaxel-Carboplatin for the First-Line Treatment of Patients With Advanced Non-Squamous Non-Small Cell Lung Cancer.	Clinical Study Report Synopsis: Protocol B7391003

4.4 The clinical trials presented in the submission formed part of the TGA submission to extrapolate Avastin's indications to Zirabev. The TGA considered the results of the 2 pharmacokinetic studies (B7391002 and B7391001), the randomised trial phase 3 clinical comparability study in the advanced NSCLC population (B7391003) and the submitted safety data supported biosimilarity between Zirabev and Avastin (TGA Delegate's Overview, pp 14 and 18).

Clinical claim

4.5 The submission claimed that Zirabev is non-inferior in terms of comparative effectiveness, and non-inferior in terms of comparative safety, to Avastin. The PBAC considered this appropriate.

Economic analysis

4.6 The minor submission proposed listing on the basis of cost-minimisation of Zirabev compared with Avastin. The equi-effective doses were estimated to be identical based on product information documents for both Zirabev and Avastin. Therefore the equi-effective doses of Zirabev and Avastin are: 100 mg of Zirabev = 100 mg of Avastin and 400 mg of Zirabev = 400 mg of Avastin.

Table 2. Requested price for Zirabev (bevacizumab)

Zirabev	Presentation	AEMP (published)
	100 mg vial x 1	$303.94
	400 mg vial x 1	$1215.75

Source: Minor Submission, table 1.3.1 page 9

Estimated PBS usage & financial implications

4.7 The submission considered Zirabev would directly replace Avastin and not change the overall use of bevacizumab on the PBS. Additionally, the submission noted that the listing of Zirabev on the PBS at lower than the current price of Avastin, due to the application of the first new brand statutory price reduction, would deliver savings to Commonwealth.

4.8 As a minor submission, the financial estimates have not been independently evaluated.

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

5 PBAC Outcome

5.1 The PBAC recommended the listing of the biosimilar brand of bevacizumab, Zirabev, on the basis that it should only be available under special arrangements under Section 100 (Efficient Funding of Chemotherapy) for all of the indications for which the reference brand, Avastin, is currently PBS-listed.

5.2 The PBAC recommended listing Zirabev 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 Zirabev is not expected to grow the market.

5.3 The PBAC noted that the TGA determined Zirabev to be a biosimilar to the reference brand Avastin based on the clinical evidence presented in the submission and that the extrapolation of indications for Zirabev to all the indications of Avastin in Australia was appropriate.

5.4 The PBAC noted that the biosimilar uptake driver of applying a different authority type to the biosimilar brand cannot be given effect for EFC medicines. The PBAC noted that the Authority Required (STREAMLINED) listing for all indications, except for relapsed or recurrent glioblastoma, is appropriate given it is the least stringent authority type that can be applied to EFC drugs. However, the PBAC recommended the current authority type for the relapsed or recurrent glioblastoma indication should apply for Zirabev, which is a written authority for initial treatment and telephone authority for continuing treatment.

5.5 The PBAC recalled its advice from the July 2019 meeting that the Department develop a set of biosimilar uptake drivers suitable for EFC medicines as the current biosimilar uptake drivers cannot be applied to EFC medicines.

5.6 The PBAC noted that EFC medicines are governed by the *National Health (Efficient Funding of Chemotherapy) Special Arrangement 2011*, and that Section 33(2) allows substitution of brands under the same item code. Therefore, the Avastin and Zirabev brands of bevacizumab should be treated as equivalent to each other.

5.7 The PBAC noted that bevacizumab is not included on the list of PBS-listed drugs suitable for prescribing by nurse practitioners.

5.8 The PBAC noted that the Early Supply Rule does not currently apply to Section 100 (Efficient Funding of Chemotherapy) listings.

5.9 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Zirabev is not expected to provide a 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.

5.10 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 Add new medicinal product pack (MPP)/trade product pack (TPP) to the existing listings for bevacizumab: 11727F 11731K 11791N 11811P 10120P 10114H 7243F 10885X 11749J 11745E

Name, restriction, manner of administration, and form	Proprietary Name, Manufacturer
BEVACIZUMAB bevacizumab 100 mg/4 mL injection, 4 mL vial bevacizumab 400 mg/16 mL injection, 16 mL vial	Zirabev Pfizer Australia Pty Ltd

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

7 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.

8 Sponsor's Comment

The sponsor had no comment.