

## 5.16 TRASTUZUMAB

### **Powder for I.V. infusion 150 mg, Powder for I.V. infusion 440 mg with diluent, Ogivri<sup>®</sup>, Alphapharm Pty Ltd**

#### **1 Purpose of Application**

- 1.1 The minor submission sought an Authority Required (STREAMLINED) listing for a new biosimilar brand of trastuzumab (Ogivri<sup>®</sup>).

#### **2 Requested listing**

- 2.1 The submission requested listing Ogivri for all indications for which the reference brand Herceptin is currently PBS listed:
- HER2-positive early, locally advanced and metastatic breast cancer (MBC)
  - HER2-positive metastatic gastric cancer (MGC)
- 2.2 Ogivri is TGA approved with the same indications as the reference brand, Herceptin: early breast cancer, locally advanced breast cancer, metastatic breast cancer, and advanced gastric cancer.
- 2.3 The sponsor requested listing on the following schedules: Chemotherapy items for Public hospital use and Chemotherapy items for Private hospital use.
- 2.4 Due to the length of the proposed restrictions in the submission, a restriction summary was not been included. The sponsor requested restriction details and wording that is identical to the listings for the reference product, Herceptin.
- 2.5 The requested dispensed price for maximum quantity (DPMQ) was calculated based on the current list price for Herceptin and accounted for the 25% statutory price reduction that would occur if Ogivri is listed on the PBS.
- 2.6 The sponsor requested that Ogivri be 'a' flagged against the reference product, with Authority Required (STREAMLINED) listings across all item codes.
- 2.7 The item codes relating to the Herceptin SC (subcutaneous injection) brand are not sought for reimbursement.
- 2.8 The Herceptin and Ogivri brands share one common presentation: a single vial with 150 mg powder for reconstitution with sterile water for IV administration. Each brand also has a presentation that is not shared by the other brand: Herceptin has a 60 mg injection presentation and Ogivri a 440 mg Pharmacy Bulk Pack presentation.

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

### **3 Background**

3.1 The Ogivri brand of trastuzumab was TGA approved on 5 December 2018 and was determined to be a biosimilar to the reference brand Herceptin.

3.2 The PBAC had not previously considered a submission for this brand of trastuzumab.

#### ***Brand equivalence and substitution at the pharmacist level ('a' flagging)***

3.3 The sponsor requested that Ogivri be 'a' flagged against the reference product, Herceptin.

#### ***Biosimilar uptake measures***

3.4 The sponsor requested Authority Required (STREAMLINED) listings across all item codes for Ogivri. Herceptin has an Authority Required (Written) and Authority Required (Telephone) listing on the PBS.

*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 biosimilarity of Ogivri and Herceptin. As this was a minor submission, no evaluation of the clinical evidence was undertaken.

Table 1: Trials and associated reports presented in the submission

Trial ID (Full Study No.)	Protocol title/publication title	Publication citation
<b>Direct randomised trial(s)</b>		
<b>MYL-Her-3001</b>	A Multicentre, Double-blind, Randomized, Parallel-group, Phase III Study of the Efficacy and Safety of Hercules Plus Taxane Versus Herceptin® Plus Taxane as First Line Therapy in Patients With HER2-Positive Metastatic Breast Cancer	Clinical Study Report Report date: 7 March 2017
	<p><u>Main publication</u> Rugo HS, Barve A, Waller CF, et al. for the Heritage Study Investigators. Effect of a proposed trastuzumab biosimilar compared with trastuzumab on overall response rate in patients with ERBB2 (HER2)-positive metastatic breast cancer: a randomized clinical trial.</p> <p><u>Additional citations</u> Rugo HS, Barve A, Waller CF, et al. Heritage: A phase III safety and efficacy trial of the proposed trastuzumab biosimilar Myl-1401O versus Herceptin.</p> <p>Rugo H, Barve A, Waller CF, et al. Heritage, a phase III safety and efficacy trial of the proposed trastuzumab biosimilar, Myl-1401O vs trastuzumab.</p>	<p><i>JAMA</i>. 2017; 317(1):37-47.</p> <p><i>J Clin Oncol</i>. 2016; 34(suppl; abstr LBA503).</p> <p><i>Ann Oncol</i>. 2016; 27(6):1-36.</p>
<b>Supporting evidence</b>		
<b>BM200-CT3-001-11</b>	Comparative PK, Efficacy, Safety and Immunogenicity evaluation of Bmab-200 versus Herceptin®, both in combination with Docetaxel in patients with Her2+ Metastatic Breast Cancer: A Double Blind, Randomised, Active Control, Parallel assignment, Comparative Phase III Clinical Trial Short Title: Bioequivalence of Bmab-200 with Herceptin®	Clinical Study Report Report date: 3 October 2013

Source: Table 2.2 of the submission, page 37

- 4.4 The clinical trials presented in the submission formed part of the sponsor’s TGA documentation, i.e. the summary of clinical efficacy of Ogivri. These comprised one head-to-head pivotal trial comparing Ogivri to Herceptin in patients with HER2-positive MBC, and one supportive trial conducted with Bmab-200 (an older formulation of trastuzumab identical to Herceptin) versus Herceptin in patients with HER2-positive metastatic breast cancer.
- 4.5 Study MYL-Her-3001 was a multicentre, double-blind, randomised, parallel-group, Phase III study to compare the efficacy and safety of Ogivri (MYL-1401O) versus Herceptin in patients with HER2-positive MBC.
- 4.6 The results of the primary analysis demonstrated the following. At Week 24, the overall response rate (ORR) in the Ogivri group was 69.6% and 64.0% in the Herceptin group. For the primary endpoint per the Food and Drug Administration (FDA)’s recommendation, the ratio of the ORRs of Ogivri:Herceptin was 1.09 with a 90% confidence interval (CI) of (0.974, 1.211). As this CI is entirely within the pre-defined equivalence boundaries of 0.81 and 1.24, the TGA was satisfied that therapeutic

equivalence of Ogivri and Herceptin was statistically confirmed per the FDA's recommendation in this study.

- 4.7 For the primary endpoint per the European Medicines Agency (EMA)'s recommendation, the difference in best ORRs between treatment groups (Ogivri minus Herceptin) was 5.5% with a 95% CI of (-3.08%, 14.04%). As this CI is entirely within the pre-defined equivalence boundaries of -15% and 15%, the TGA was satisfied that therapeutic equivalence of Ogivri and Herceptin was statistically confirmed per EMA's recommendation in this study.
- 4.8 As secondary analyses, time to tumour progression (TTP), progression-free survival (PFS), and overall survival (OS) were evaluated at Week 24 and Week 48 for the intent-to-treat (ITT) population. Furthermore, duration of response (DR) was analysed at Week 48. The TGA was satisfied that therapeutic equivalence of Ogivri and Herceptin was statistically confirmed by the primary efficacy analysis, and that all secondary efficacy analyses at Week 24 and Week 48 supported the conclusion of therapeutic equivalence.
- 4.9 Overall, the TGA confirmed that Ogivri and Herceptin were well tolerated both in combination with a taxane and when given as monotherapy. When administered with a taxane as first-line therapy to patients with HER2-positive MBC, their safety profiles were similar and no safety concerns were observed.
- 4.10 With respect to the supporting evidence, the TGA found that Bmab-200 is bioequivalent to Herceptin and is similar in safety and efficacy parameters to Herceptin. Furthermore, the TGA was satisfied that the results of BM200-CT3-001-11 supported a claim of non-inferior safety and efficacy of Ogivri compared to Herceptin in patients with HER2-positive metastatic breast cancer.

### ***Clinical claim***

- 4.11 The submission's clinical claim was that Ogivri is non-inferior in terms of comparative effectiveness, and non-inferior in terms of comparative safety, to Herceptin.
- 4.12 The TGA was satisfied that the biosimilar brand was non-inferior in terms of both efficacy and safety compared to the reference brand.
- 4.13 The PBAC considered that the claim of non-inferior comparative effectiveness and non-inferior comparative safety was reasonable.

### ***Estimated PBS usage & financial implications***

- 4.14 The submission stated that listing Ogivri would confer cost savings to the PBS as it would trigger a 25% New Brand Statutory Price Reduction under division 3A of Part VII of the National Health Act 1953 to the ex-manufacturer price of Herceptin. The proposed listing is estimated to save the PBS/RPBS \$30 to \$60 million in Year 1, increasing to \$60 to \$100 million in Year 6 (see Table 2 below).

Table 2: Estimated net cost to the PBS/RPBS for Ogivri

	2019	2020	2021	2022	2023	2024
<b>Projected net cost of new listing: Ogivri</b>						
to PBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
to RPBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
to PBS/RPBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
<b>Projected net cost of displaced medicines: Herceptin</b>						
to PBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
to RPBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
to PBS/RPBS	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]	\$ [REDACTED]
<b>Net cost to the PBS/RPBS</b>						
to PBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
to RPBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
to PBS/RPBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
<b>Projected net cost of Herceptin not replaced with Ogivri (after 25% price cut)</b>						
to PBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
to RPBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
to PBS/RPBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
<b>Overall net cost to the PBS/RPBS</b>						
to PBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
to RPBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]
to PBS/RPBS	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]	-\$ [REDACTED]

Source: Minor submission, page 76

- 4.15 The sponsor stated that the Special Pricing Arrangement (SPA) that currently applies to Herceptin is likely to change the financial estimates presented in the submission.

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

## 5 PBAC Outcome

- 5.1 The PBAC recommended the listing of trastuzumab (Ogivri) as a biosimilar of trastuzumab (Herceptin) for all of the indications for which Herceptin is PBS-listed.
- 5.2 The PBAC noted the TGA was satisfied that the two clinical equivalence studies presented in the submission demonstrated clinical equivalence for subjects with early breast cancer, locally advanced breast cancer, metastatic breast cancer, and advanced gastric cancer. The PBAC also noted that the safety data from the trials did not show clinically significant differences in any of the safety outcomes assessed.
- 5.3 The PBAC advised that there would not be clinical or other concerns about appropriate use of medicines if a policy decision were made to lower the authority requirement for the reference biological medicine to align with the biosimilar brand(s).
- 5.4 The PBAC considered that, upon PBS listing of a biosimilar brand, it would be suitable for all trastuzumab listings, across all indications, to be made Authority Required (STREAMLINED), with a change in wording to allow adjuvant or neoadjuvant treatment

for early breast cancer, and to allow treatment in combination with any platinum chemotherapy for advanced gastric cancer. The PBAC also recommended the removal of the ‘locally advanced’ indication and for the written authority requirement to remain for pertuzumab, trastuzumab emtansine and lapatinib in metastatic breast cancer.

- 5.5 The PBAC advised that, under Section 101(4AACD) of the *National Health Act, 1953*, in the Schedule of Pharmaceutical Benefits, Ogivri and Herceptin intravenous injections should be treated as equivalent to each other.
- 5.6 The PBAC also considered that application of biosimilar uptake drivers would be appropriate.
- 5.7 The PBAC reiterated its previous advice that trastuzumab should be exempt from the Early Supply Rule.
- 5.8 The PBAC reiterated its previous advice that trastuzumab is not suitable for prescribing by nurse practitioners.
- 5.9 The PBAC noted this recommendation does not include the drug trastuzumab emtansine.
- 5.10 The PBAC noted that this submission is not eligible for an Independent Review as it was a positive recommendation.

**Outcome:**

Recommended

## **6 Recommended listing**

- 6.1 Restriction to be finalised.

## **7 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.

## **8 Sponsor’s Comment**

The sponsor had no comment.