

5.28 TRASTUZUMAB, Powder for I.V. infusion 440 mg, Herzuma[®], Celltrion Healthcare Australia Pty Ltd

1 Purpose of Submission

- 1.1 The Committee Secretariat submission sought Section 100 Efficient Funding of Chemotherapy (S100 EFC) Authority Required (STREAMLINED) listing of a new vial size containing 440 mg trastuzumab, Herzuma[®] (herein referred to as Herzuma 440 mg) under the same circumstances as the current trastuzumab 60 mg, 150 mg and 420 mg listings.

2 Background

- 2.1 Herzuma 440 mg was TGA approved on 20 April 2020 as a biosimilar trastuzumab product, with identical indications to the PBS-listed Herzuma 150 mg injection.
- 2.2 The reference biologic, Herceptin[®], was delisted from the PBS on 1 October 2021.
- 2.3 Trastuzumab is listed on the PBS for the treatment of:
- metastatic (Stage IV) HER2 positive breast cancer
 - metastatic (Stage IV) HER2 positive adenocarcinoma of the stomach or gastro-oesophageal junction
 - Early HER2 positive breast cancer
 - Locally advanced HER2 positive breast cancer.
- 2.4 Trastuzumab 60 mg and 150 mg are available in various brands, including Herzuma, Ogivri[®], Ontruzant[®] and Trazimera[®]. Trastuzumab 420 mg is available in one brand only (Kanjinti[®]).
- 2.5 The PBAC noted EFC medicines are governed by the *National Health (Efficient Funding of Chemotherapy) Special Arrangement 2011* and subsection 33(2) allows substitution of brands with the same chemotherapy drug.

For more detail on PBAC's view, see section 7 PBAC outcome.

3 Requested listing

- 3.1 The submission requested listing of Herzuma 440 mg injection under the same circumstances as trastuzumab 60 mg, 150 mg and 420 mg. The submission proposed no changes to the existing restriction.
- 3.2 The submission requested a new trade product pack of Herzuma 440 mg injection (1 vial) be added to the existing PBS item codes: 4632T; 4639E; 4650R; 4703M; 7264H; 7265J; 7266K; 7267L; 10383L; 10391X; 10401K; 10402L; 10581X; 10588G; 10589H and 10597R.
- 3.3 The restrictions have not been reproduced due to their length. The sponsor requested restriction details and wording that is identical to the existing trastuzumab listings.

For more detail on PBAC's view, see section 7 PBAC outcome.

4 Comparator

- 4.1 The submission nominated Herzuma 150 mg vial, Herceptin and other trastuzumab biosimilars as the comparators. The PBAC considered this was appropriate.

For more detail on PBAC's view, see section 7 PBAC outcome.

5 Consideration of the evidence

Sponsor hearing

- 5.1 There was no hearing for this item.

Consumer comments

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

Clinical studies

- 5.3 The submission presented a phase 3, double-blind, randomised, parallel-group, active controlled study. The submission claimed that this study provides pivotal evidence supporting the claim of non-inferior efficacy and safety of Herzuma 440 mg compared to Herceptin in patients with HER2 positive early breast cancer.
- 5.4 The submission did not provide any other evidence to support its claim of non-inferior efficacy and safety of Herzuma 440 mg compared to Herceptin in treatment of locally advanced (Stage IIIB) or metastatic (Stage IV) HER2 positive breast cancer, or metastatic (Stage IV) HER2 positive adenocarcinoma of the stomach or gastro-oesophageal junction.

Table 1: Study presented in the submission

Trial ID/First Author	Protocol title/ Publication title	Publication citation
CT-P6 3.2 (NCT02162667)	Phase 3, Double-Blind, Randomized, Parallel-Group, Active-Controlled Study to Compare the Efficacy and Safety of CT-P6 and Herceptin as Neoadjuvant and Adjuvant Treatment in Patients with HER2-Positive Early Breast Cancer	Stebbing J, Baranau Y, Baryash V, Manikhas A, Moiseyenko V, Dzagnidze G, et al. Lancet Oncol. 2017;18(7):917-928

Source: Table 2.3, page 31 of submission

- 5.5 As a Committee Secretariat submission, no evaluation of the clinical evidence was undertaken.

Clinical claim

- 5.6 The submission claimed that Herzuma 440 mg was biosimilar to Herceptin. The PBAC considered that Herzuma 440 mg was biosimilar to Herceptin based on the TGA approved Product Information.
- 5.7 The submission claimed that on a mg for mg basis Herzuma 440 mg is non-inferior to trastuzumab 60 mg, 150 mg and 420 mg in terms of both clinical efficacy and safety.
- 5.8 The submission claimed that the equi-effective doses is that 1 mg of trastuzumab in Herzuma 440 mg is equivalent to 1 mg of trastuzumab in any other trastuzumab presentation.

Clinical need

- 5.9 The submission stated that Herzuma 440 mg provides alternative large vial size to trastuzumab 420 mg vial (Kanjinti®), which is useful when preparing higher dose infusions, for example the 8 mg/kg loading dose.
- 5.10 The submission claimed that Herzuma 440 mg is the only multiuse vial that is stable after reconstitution for up to 28 days when stored refrigerated at 2 °C to 8 °C because it contains preservative. In addition, the submission claimed that the 440 mg strength will reduce waste, improve efficiency in dose preparation and reduce risk of contamination and dosing error. The PBAC considered this could also be achieved by the existing PBS-listed trastuzumab 420 mg.

For more detail on PBAC's view, see section 7 PBAC outcome.

6 Estimated PBS utilisation and financial implications

- 6.1 The submission used a market share approach to estimate the usage of Herzuma 440 mg. The submission considered current growth of the market is not expected to change with a PBS listing of Herzuma 440 mg, assuming that the replacement of trastuzumab with Herzuma 440 mg will be on a 1:1 basis in terms of script volume.
- 6.2 The proposed approved ex-manufacturer price (AEMP) for Herzuma 440 mg was based on the AEMP of Herzuma 150 mg in June 2021. The submission stated that the

proposed AEMP for Herzuma 440 mg has been calculated based on the same price per mg of trastuzumab.

- 6.3 The submission acknowledged that there would be a price reduction to trastuzumab effective from 1 October 2021. Prior to 1 October 2021, the AEMP for Herzuma 150 mg was \$375.39, which provided a price of \$2.5026 per mg. Based on this price, the proposed AEMP for Herzuma 440 mg was \$1101.14.
- 6.4 From 1 October 2021, the AEMP of trastuzumab 150 mg reduced to \$315.26 (\$2.1017 per mg). Based on this, the AEMP for Herzuma 440 mg would be \$924.76.
- 6.5 The submission claimed that the dispensed price for maximum amount (DPMA) of 500 mg and 1000 mg are expected to reduce because there is a reduction in wastage. This claim is inappropriate because the DPMA is determined by a range of factors which do not include the reduction in wastage.
- 6.6 The submission claimed that the listing of Herzuma 440 mg will be cost neutral, because the proposed price is based on an equivalent price per mg, compared with Herzuma 150 mg.
- 6.7 The submission indicated that the alignment of the Herzuma 440 mg price with other trastuzumab vials/brands means that any change in the relative market share of trastuzumab forms will not affect the net financial impact.
- 6.8 The submission stated that the proposed listing of Herzuma 440 mg is estimated to save the PBS/RPBS \$0 to < \$10 million in Year 1, increasing to \$0 to < \$10 million in Year 6. The submission claimed that these estimates did not account for the anticipated price disclosure reductions effective from 1 October 2021.
- 6.9 As a Committee Secretariat submission, the financial estimates have not been independently evaluated.

For more detail on PBAC's view, see section 7 PBAC outcome.

7 PBAC Outcome

- 7.1 The PBAC recommended the listing of of a new vial size of 440 mg trastuzumab (Herzuma 440 mg) as S100 EFC Authority Required (STREAMLINED) under the same conditions as the currently trastuzumab 60 mg, 150 mg and 420 mg listings. The PBAC's recommendation for listing was based on, among other matters, its assessment that the cost-effectiveness of Herzuma 440 mg would be acceptable if it was cost-minimised to trastuzumab 60 mg, 150 mg and 420 mg for the indications listed under the following PBS codes: 4632T; 4639E; 4650R; 4703M; 7264H; 7265J; 7266K; 7267L; 10383L; 10391X; 10401K; 10402L; 10581X; 10588G; 10589H and 10597R.
- 7.2 The PBAC accepted that 1 mg of trastuzumab in Herzuma 440 mg is equivalent to 1 mg of trastuzumab in any other trastuzumab presentation.

Public Summary Document – November 2021 PBAC Meeting

- 7.3 The PBAC considered that the clinical claim of non-inferior comparative effectiveness and non-inferior comparative safety between Herzuma 440 mg trastuzumab 60 mg, 150 mg and 420 mg were reasonable.
- 7.4 The PBAC considered Herzuma 440 mg would provide an alternative large vial size to trastuzumab 420 mg vial (Kanjinti).
- 7.5 The PBAC considered the proposed price of Herzuma 440 mg, which was based on the same price per mg as the currently listed 150 mg, was appropriate.
- 7.6 The PBAC considered the financial estimates model presented in the submission to support its claim of a cost save is inaccurate.
- 7.7 The PBAC noted the listing of Herzuma 440 mg would be cost neutral to the government.
- 7.8 The PBAC noted that its recommendation was on a cost-minimisation basis and advised that, because Herzuma 440 mg is not expected to provide a substantial and clinically relevant improvement in efficacy, or reduction of toxicity over currently trastuzumab listings, 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.
- 7.9 The PBAC noted that this submission is not eligible for an Independent Review as it received a positive recommendation.

Outcome:

Recommended

8 Recommended listing

- 8.1 Add new medicinal pack, (trastuzumab powder for I.V. infusion 440 mg under the same circumstances as the current trastuzumab 60 mg, 150 mg and 420 mg listings as follows:

MEDICINAL PRODUCT medicinal product pack	PBS item code	Proprietary Name, Manufacturer
TRASTUZUMAB Trastuzumab powder for I.V. infusion 440 mg	4632T; 4639E; 4650R; 4703M; 7264H; 7265J; 7266K; 7267L; 10383L; 10391X; 10401K; 10402L; 10581X; 10588G; 10589H and 10597R	Herzuma Celltrion Healthcare 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.

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

The Sponsor thanks the PBAC for its deliberations.