5.17 TRASTUZUMAB
Powder for I.V. infusion 150 mg, Ontruzant®, Merck Sharp & Dohme (Australia) Pty Limited

1 Purpose of Application

1.1 The minor submission sought a Restricted Benefit listing for a new biosimilar brand of trastuzumab (Ontruzant®).

2 Requested listing

2.1 The submission requested listing Ontruzant 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 Ontruzant 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. The minor submission only included essential elements of the requested listing; there was no restriction wording proposed.

2.4 The requested dispensed price for maximum quantity was calculated based on the current list price for Herceptin and accounted for the 25% statutory price reduction that would occur if Ontruzant is listed on the PBS.

2.5 The sponsor requested that Ontruzant be listed on the PBS with a Restricted Benefit listing across all indications and treatment phases to encourage biosimilar uptake. The submission did not specifically request that Ontruzant be 'a' flagged against the reference product.

2.6 The item codes relating to the Herceptin SC (subcutaneous injection) brand are not sought for reimbursement.

2.7 The Herceptin and Ontruzant brands share one common presentation: a single vial with 150 mg powder for reconstitution with sterile water for IV administration. Herceptin also has a 60 mg injection presentation that is not shared by Ontruzant.

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

3 Background

3.1 The Ontruzant brand of trastuzumab was TGA approved on 9 January 2019 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 pre-PBAC response requested that Ontruzant be 'a' flagged against the reference product, Herceptin.

Biosimilar uptake measures

3.4 The sponsor requested that Ontruzant be listed on the PBS with a Restricted Benefit listing across all indications and treatment phases, i.e. a reduced level of authority to encourage biosimilar uptake, while retaining physician and patient choice. 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 one randomised controlled trial comparing the biosimilarity of Ontruzant and Herceptin in early or locally advanced HER2-positive breast cancer treated with neoadjuvant-adjuvant treatment. 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
Direct randomised trial(s)		
SB3-G31-BC	A Phase III Randomised, Double-Blind, Parallel Group, Multicentre Study to Compare the Efficacy, Safety, Pharmacokinetics and Immunogenicity Between SB3 (Proposed Trastuzumab Biosimilar) and Herceptin® in Women With Newly Diagnosed HER2 Positive Early or Locally Advanced Breast Cancer in Neoadjuvant Setting	N/A

Source: Page 9 of the Delegate's Overview provided with the minor submission

4.4 The primary efficacy endpoint was the pathological complete response rate of the primary breast tumour (bpCR). The adjusted ratio was found to be 1.259 with a 90% confidence interval (CI) of (1.112, 1.426) which the TGA Delegate found to be entirely contained within the pre-defined equivalence margin of (0.785, 1.546).

4.5 The secondary efficacy endpoints included total pathological complete response (tpCR) rate, overall clinical response rate, event-free survival and overall survival. The Delegate's overview states that over 90% of patients achieved complete or partial response in both treatment groups. The overview also found that overall response rates and tpCRs were comparable between the two treatment groups.

4.6 The Delegate found that the incidence of any adverse effects was comparable between the Ontruzant and Herceptin treatment groups during the overall study period. A total of 426 (97.5%) subjects in the Ontruzant treatment group and 421 (96.1%) in the Herceptin treatment group reported at least one treatment-emergent adverse event (TEAE), with the overview concluding that the incidence of specific TEAEs was similar across the treatment groups.

4.7 The sponsor requested to extrapolate the results of the trial to all approved Herceptin indications, including metastatic breast cancer and metastatic gastric cancer.

Clinical claim

4.8 The submission's clinical claim was that Ontruzant is non-inferior in terms of comparative effectiveness, and non-inferior in terms of comparative safety, to Herceptin.

4.9 The TGA was satisfied that the biosimilar brand was non-inferior in terms of both efficacy and safety compared to the reference brand.

4.10 The PBAC considered that the claim of non-inferior comparative effectiveness and non-inferior comparative safety was reasonable.

Estimated PBS usage & financial implications

4.11 The submission stated that listing Ontruzant would confer cost savings to the PBS as it would trigger a New Brand Statutory Price Reduction under division 3A of Part VII of the National Health Act 1953. The submission did not attempt to quantify the savings.

4.12 The sponsor noted that Herceptin is subject to a Special Pricing Arrangement (SPA) and, as such, the proposed AEMP might not reflect the true effective price of trastuzumab.

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

5 PBAC Outcome

5.1 The PBAC recommended the listing of trastuzumab (Ontruzant) as a biosimilar of trastuzumab (Herceptin) for all of the indications for which Herceptin is PBS-listed.

5.2 The PBAC noted the TGA Delegate did not have concerns around the clinical equivalence of Ontruzant with respect to Herceptin for early breast cancer, locally advanced breast cancer, metastatic breast cancer, and advanced gastric cancer. The

PBAC also noted that the safety data from the key trial did not show clinically significant differences in any of the safety outcomes assessed.

5.3 The PBAC advised 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 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, Ontruzant 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.