Record of the ad hoc Cancer Treatments Advisory Committee
Meeting held on 27 January 2023 via Zoom

The Cancer Treatments Advisory Committee (CTAC) records are published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) Specialist Advisory Committees 2021.

Note that this document is not necessarily a complete record of the Cancer Treatments Advisory Committee meeting; only the relevant portions of the meeting record relating to Cancer Treatments Advisory Committee discussions about an application or Pharmac staff proposal that contain a recommendation are generally published.

The Cancer Treatments Advisory Committee may:

(a) recommend that a pharmaceutical be listed by Pharmac on the Pharmaceutical Schedule and the priority it gives to such a listing;

(b) defer a final recommendation, and give reasons for the deferral (such as the supply of further information) and what is required before further review; or

(c) recommend that Pharmac decline to list a pharmaceutical on the Pharmaceutical Schedule.

Pharmac Advisory Committees make recommendations, including priority, within their therapeutic groups of interest.

The record of this Advisory Committee meeting will be reviewed by PTAC at an upcoming meeting.

Specialist Advisory Committees and PTAC may differ in the advice they provide to Pharmac, including recommendations' priority, due to the committees' different, if complementary, roles, expertise, experience, and perspectives.

Pharmac is not bound to follow the recommendations made below. Applications are prioritised by Pharmac against other funding options and progressed accordingly. The relative priority of anyone funding choice is dependent on a number of factors, including (but not limited to) the recommendation of PTAC and/or Specialist Advisory Committees, the mix of other applications being assessed, the amount of funding available, the success of commercial negotiations and/or the availability of clinical data.

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1. Attendance

Present
Chair Stephen Munn (chair for parts of)
Alice Loft
Anne O'Donnell
Chris Hemmings
Chris Frampton
Matthew Strother (chair for parts of)
Michelle Wilson
Lochie Teague

Apologies
Allanah Kilfoyle
Peter Ganly

2. Summary of recommendations

Pharmaceutical and Indication	Recommendation
• Retreatment with trastuzumab following disease progression in metastatic breast cancer	Decline

3. The role of Specialist Advisory Committees and records of meetings

3.1. This meeting record of the Cancer Treatments Advisory Committee is published in accordance with the Terms of Reference for the Pharmacology and Therapeutics Advisory Committee (PTAC) and Specialist Advisory Committees 2021, available on the Pharmac website at https://pharmac.govt.nz/assets/2021-Specialist-Advisory-Committee-Terms-of-Reference.pdfThe Terms of Reference describe, *inter alia*, the establishment, activities, considerations, advice, and the publication of such advice of Specialist Advisory Committees and PTAC.

3.2. Conflicts of Interest are described and managed in accordance with section 7.2 of the PTAC Terms of Reference.

3.3. The Cancer Treatments Advisory Committee is a Specialist Advisory Committee of Pharmac. The Cancer Treatments Advisory Committee and PTAC and other Specialist Advisory Committees have complementary roles, expertise, experience, and perspectives. The Cancer Treatments Advisory Committee and other Specialist Advisory Committees may therefore, at times, make recommendations for treatments for cancer that differ from PTAC's, including the priority assigned to recommendations, when considering the same evidence. Likewise, PTAC may, at times, make recommendations for treatments that differ from the Cancer Treatments Advisory Committee's, or Specialist Advisory Committees may make recommendations that differ from other Specialist Advisory Committees'.

3.4. Pharmac considers the recommendations provided by both the Cancer Treatments Advisory Committee and PTAC and any other relevant Specialist Advisory Committees when assessing applications for treatments.

4. Correspondence and Matters Arising

4.1. Matters Arising – Supply issues management

Discussion

4.1.1. The Committee noted the recent supply issue for capecitabine. The Committee considered there to be ambiguity about how former entities of DHBs interacted with Pharmac compared to the current whole of system approach. The Committee considered that this was a particularly difficult supply issue to manage because there is variability across the country regarding how this cytotoxic is dispensed, with some regions dispensing through community pharmacy and others through hospital pharmacy.

4.1.2. The Committee noted that this did lead to several requests to cover other regions' needs for medicine because there was insufficient reserves in all regions at the time of the supply issue. The Committee considered the impact of supply issues on healthcare professionals can be large, particularly given the constraints already experienced by many parts of the sector. The Committee considered it unclear how this communication was fed back to Pharmac and who communicates with the clinicians and pharmacists so that there is a more all of system approach.

4.1.3. The Committee considered that the time of year also compounded this issue and that this likely created difficulty in the management of supply. The Committee considered it important for Pharmac to understand what the communication chains are for supply issues, as and when they do occur. The Committee considered that it would be useful to explore broader communication networks for these sorts of issues to avoid the need for this to be managed by the centres working at or near capacity to explain national medicines supply issues.

4.1.4. The Committee considered that it would be useful to obtain feedback from Pharmac around how further mitigations would be put in place for the maintenance of supply and for communication of supply issues given the significant impact that this supply issue had on the oncology services across the country.

4.2. Matters Arising – Consultation feedback for immune checkpoint inhibitors for advanced NSCLC

Discussion

4.2.1. The Committee noted that some specific feedback was received from the Lung Oncology Special Interest Group (LOSIG) in response to the consultation released on 16 December 2022 to fund immune checkpoint inhibitors for the treatment of advanced non-small cell lung cancer.

4.2.1.1. The Committee noted that there was a request that the renewal criteria for access to immune checkpoint inhibitors be amended to align with the immune related RECIST criteria (iRECIST).

4.2.1.1.1. The Committee noted that none of the clinical trials (KEYNOTE 024, KEYNOTE 189, KEYNOTE 407and OAK) for the relevant agents reported on iRECIST as an endpoint, however they were co-developing iRECIST as a criteria within these trials and hence this information was captured.

4.2.1.1.2. The Committee considered that the criteria proposed as part of this proposal had been recommended specifically, as a pragmatic move away from RECIST criteria and to facilitate equitable and consistent access to treatment. The Committee considered that this request created tension

between this intent and attempting to differentiate between actual disease progression and pseudoprogression.

4.2.1.1.3. The Committee considered that it would be useful to review pseudoprogression and its impact on people receiving immunotherapy at a future meeting of CTAC and welcomed information from the relevant interest groups (melanoma and lung) to support such considerations.

4.2.1.2. The Committee noted that there was a request that access be enabled for those patients who are contraindicated to chemotherapy with PD-L1 positivity (≥1%).

4.2.1.2.1. The Committee considered that the proposed criteria include the ability to access treatment for those who are unable to obtain sufficient tissue to biopsy. The Committee considered that the majority of people who were unable to obtain sufficient tissue to biopsy would be included in the group with contraindications to chemotherapy. The Committee considered that enabling funded access for circumstances where sufficient tissue cannot be obtained is a reasonable request in the context of a rapidly progressing disease, as considered previously (October 2022).

4.2.1.2.2. The Committee considered that it would be very difficult to find evidence for people who are contraindicated to chemotherapy, as they were often specifically excluded from the clinical trials for immunotherapy. However the Committee considered this group reflects a real-world population that could benefit from treatment. The Committee considered that Māori and Pacific peoples are likely to be overrepresented in this group and therefore enabling funded access would support achieving equitable health outcomes for people with advanced lung cancer.

4.2.1.2.3. The Committee noted the proposed criteria for those receiving monotherapy included a requirement of PD-L1 expression at a level of 50% or greater, however considered there is evidence that people with a positive PD-L1 expression (ie of 1-49%) would also receive benefit. Therefore, the Committee considered it would be reasonable to enable funded access to immunotherapy for those with a PD-L1 expression of 1-49%. The Committee noted that those who do not receive benefit would not be eligible for ongoing funded access given the proposed renewal criteria.

4.2.1.2.4. The Committee noted that the proposed criteria include only those with a performance status (ECOG) of 0-2 and therefore those classified as having poor performance status (ie ECOG higher than 2) would not be eligible for treatment. The Committee considered that the community is aware of the potential benefit that immunotherapy would provide for these patients. The Committee considered that in practice, this group whose performance status suggests that chemotherapy is not in their best interest would likely still access immunotherapy via the current eligibility criteria, through a reduced dose of combination chemotherapy. The Committee considered that enabling access to monotherapy for this patient group with PD-L1 positivity would not present a significant fiscal risk, given the previous considerations, however it would simplify the process for people to receive monotherapy and eliminate the risk of side effects from the combination chemotherapy (if even administered at a reduced dose).

4.2.1.2.5. The Committee considered that most clinicians would want information regarding PD-L1 status to inform on treatment decisions and therefore testing would be requested for all individuals. The Committee re-iterated the significant impact that PD-L1 testing would have on the pathology service

as it is a resource intensive process, and there may be impacts for other services after the supplier funded testing ends.

4.2.1.2.6. The Committee considered that if there was a delay in accessing PD-L1 testing results after the bridging funding put in place by the supplier, there would be instances of clinicians ordering the test and then treating while they are waiting for the result. The Committee considered that such practice to start with combination therapy and then remove the chemotherapy component if there was a positive PD-L1 test was not uncommon internationally.

4.2.1.3. The Committee considered that clinicians would work pragmatically in interpreting the eligibility criteria.

4.2.2. The Committee noted a request to make certain monoclonal antibodies available specifically for the management of immune related adverse events.

4.2.2.1. The Committee considered that this would best be addressed by the Medical Oncology Working Group as there is not complete representation of all centres on the Committee.

4.2.2.2. The Committee noted that this was a specific concern when immunotherapy was funded for people with metastatic melanoma. The Committee considered that this concern has not eventuated and that there have been nominal numbers of patients who have required these treatments for the management of adverse events. The Committee considered that this has been managed appropriately through Pharmac's exceptional circumstances framework. The Committee considered that this would remain appropriate should immunotherapy be funded for NSCLC.

4.2.3. The Committee noted a request for those who have received two or more prior lines of treatment be eligible for immunotherapy with atezolizumab.

4.2.3.1. The Committee considered that it had specifically reviewed those who had received more than one prior line of treatment, and that this group had been included in the estimate of the prevalent bolus referenced in the April 2022 CTAC record. The Committee considered that those who had received multiple prior lines of treatment would contribute to a small proportion of the overall population.

5. Trastuzumab biosimilar

Application

5.1. The Advisory Committee reviewed the clinical evidence for a trastuzumab biosimilar (brand name Trazimera) in the treatment of breast cancer, as part of an ongoing competitive process for the supply of intravenous trastuzumab.

5.2. The Advisory Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

5.3. The Committee considered that it would be clinically acceptable if Trazimera were the only available trastuzumab brand (principal supply) for the indications for which trastuzumab is currently funded.

5.4. The Committee considered that the available evidence indicates that there would be minimal risk if Pharmac decided to transition from the currently funded trastuzumab brand to Trazimera.

Discussion

Background

5.5. The Committee noted that in 2019, both PTAC and CTAC (previously CaTSoP) reviewed an application for the trastuzumab biosimilar CT-P6 (Herzuma) for the treatment of HER2-positive early breast cancer and HER2-positive metastatic breast cancer. The Committee noted that PTAC was supportive of Pharmac progressing a competitive procurement process for trastuzumab and considered that a managed change to a single trastuzumab biosimilar product, such as CT-P6, would be clinically acceptable for the treatment of HER2-positive early breast cancer and HER2-positive metastatic breast cancer.

5.6. The Committee noted that, at the discussion in 2019, it considered that there is no evidence to suggest any differences in the health benefits or risks between reference and biosimilar trastuzumab, and recommended it was clinically acceptable for a biosimilar trastuzumab, such as CT-P6, to be listed and be the only available trastuzumab product for all funded indications, if the cost saving is worthwhile and supply is secured. The Committee also noted that in 2019 it supported a competitive process and recommended that Pharmac bring any other biosimilar trastuzumab options to CaTSoP, when available in future, for review.

5.7. The Committee noted the competitive process for intravenous trastuzumab was ongoing. Pharmac staff were seeking the Committee's review on a biosimilar brand, Trazimera, as part of its evaluation and no decisions had been made regarding a potential outcome.

Health need

5.8. The Committee considered that the health need associated with HER2 positive early and metastatic breast cancer has already been established as reference trastuzumab (Herceptin) is already funded for these indications.

Health benefit

5.9. The Committee noted that Trazimera is a humanized antibody against human epidermal growth factor receptor 2 protein (HER2) is produced by recombinant mammalian cells (Chinese hamster ovary (rch)) in suspension culture in a nutrient medium. The Committee noted that Trazimera is indicated for the treatment of patients with metastatic breast cancer who have tumours that overexpress HER2, and the treatment of patients with early breast cancer with HER2-positive locally advanced breast cancer in combination with neoadjuvant chemotherapy, followed by adjuvant Trazimera or HER2-positive early breast cancer following surgery, sequentially or concurrently with chemotherapy and, if applicable, radiotherapy.

5.10. The Committee noted that although Trazimera has undergone regulatory approval in New Zealand as a trastuzumab biosimilar product, it was not aware if Trazimera is considered to be an "interchangeable" biosimilar in the New Zealand context (ie can be substituted for the reference product without pausing treatment, and without any change in clinical effect). The Committee noted that different jurisdictions globally have differing requirements for evidence of interchangeability and that this would need to be considered ahead of any future processes that may result in a change from biosimilar to biosimilar.

5.11. The Committee noted the following clinical evidence relating to the biosimilarity of Trazimera:

5.11.1. REFLECTIONS B327-01 (Yin et al. Br J Clin Pharmacol. 2014;78:1281-90): a phase I randomised, single dose trial comparative pharmacokinetic study in

which 105 males were given one dose of Trazimera (n=34), US Herceptin (N=32) or EU Herceptin (n=35). Trazimera met the endpoint of bioequivalence (within a window of 80-125% for pharmacokinetic parameters). The study was not powered for adverse events, anti-drug antibody detection, or neutralising antibodies. The study also did not provide any information regarding combined therapies.

5.11.2. REFLECTIONS B327-02 (Pegram et al. Br J Cancer. 2019;120:172-82): a phase III randomised, double-blind study in which females with metastatic, HER2-positive breast cancer were treated with either Trazimera or EU Herceptin administered weekly in combination with paclitaxel. The study met its endpoint for bioequivalence with partial and complete response at week 25. The study was not powered for adverse events, anti-drug antibody detection, or neutralising antibodies.

5.11.3. REFLECTIONS B327-02 (Li et al. BioDrugs. 2022;36:55-69): long term results – six-year follow-up. The overall survival was numerically similar between treatment groups, but the study was not powered for statistical significance. There were no emergent adverse events reported.

5.11.4. REFLECTIONS B327-02 (Chen et al. Cancer Chemother Pharmacol. 2019;84:83-92): Population pharmacokinetics study to explore variation in baseline covariate effects. No difference in covariate effects between products was reported.

5.11.5. REFLECTIONS B327-04 (Lammers et al. BR J Cancer. 2018;119:266-73): a randomised, parallel assignment, double-bind phase III trial of women with HER2-positive invasive breast cancer treated with either Trazimera or EU-Herceptin as neoadjuvant therapy in combination with chemotherapy. Trazimera was reported to be non-inferior (via Ctrough), although data for clinical endpoints was not reported.

5.12. The Committee considered that overall the studies were of good quality. The Committee considered that pharmacokinetic parameters between Trazimera and Herceptin were shown to be bioequivalent. The Committee noted that there is no evidence regarding the combination of Trazimera with other HER2-targeted monoclonal antibody treatments, and there is limited information relating to switching between trastuzumab agents part-way through treatment.

5.13. The Committee noted that although there is no direct evidence relating to switching between Herceptin and Trazimera, there is some evidence relating to trastuzumab switching with other products:

5.13.1. Hester et al. Geburtshilfe Frauenheilkd. 2020;80:924-31: A German observational cohort with majority switching between intravenous Herceptin to intravenous Kanjinti (trastuzumab biosimilar). Approximately half of the cohort were also being treated with pertuzumab (primarily in the metastatic setting). There were no new or unexpected adverse events reported, and the rate of response was similar to that of historic cohorts.

5.13.2. Saito et al. Biol Pharm Bull. 2021;44:474-77: a Japanese cohort with breast cancer or gastric cancers who received CT-P6 (trastuzumab biosimilar) as a 30 minute infusion as cycle one of a switch from reference trastuzumab. The rate of infusion reactions was reported to be within historically expected rates.

5.13.3. Declerck et al. Clin Ther. 2018;40:798-809: a critical appraisal of clinical evidence for switching in oncology which identified only one trastuzumab switching study (LILAC study).

5.13.4. LILAC study (Minckwitz et al. Lancet Oncol. 2018;19:987-98): a study of neoadjuvant ABP (trastuzumab biosimilar) versus Herceptin in the treatment of patients with HER2-positive early breast cancer in the adjuvant setting (switch as part of the post-operative period). The study was unpowered to find statistically significant differences between the two products in terms of clinical endpoints. There was no difference between the two products in the total trastuzumab completed, or adverse events.

5.14. The Committee noted the following evidence relating to biosimilars in combination with other HER2-targeted monoclonal antibodies:

5.14.1. Suppan et al. Breast Care (Basel). 2021;16:607-13: a study of an Austrian cohort treated with Herzuma (trastuzumab biosimilar) in combination with pertuzumab in the treatment of HER2-positive breast cancer patients in the neoadjuvant and metastatic setting. There were numerically similar rates of adverse evets reported.

5.14.2. Bae et al. Front Oncol. 2021;11:689587: a South Korean cohort of HER2-positive early breast cancer patients treated with CT-P6 and pertuzumab in the metastatic and neoadjuvant setting. The study reported numerically similar progression free survival and pathologic complete response in the neoadjuvant setting compared to a Herceptin control.

5.14.3. Hanes et al. Cancer Chemother Pharmacol. 2021;88:879-86: a two-arm randomised controlled trial of Kanjinti versus Herceptin (in combination with pertuzumab) in healthy volunteers. There was no difference in safety or tolerability reported.

5.14.4. Celik et al. Breast Cnacer (Auckl). 2022;16:11782234221086992: a Danish cohort of metastatic breast cancer patients treated with Sb3 (trastuzumab biosimilar) and pertuzumab. The study reported numerically similar progression free survival to historical data of Herceptin in combination with pertuzumab.

5.14.5. Berg et al. Breast. 2020;54:242-7: a Danish cohort of early breast cancer patients treated with Sb3 and pertuzumab. The study reported numerically similar pathological complete response compared to historic Herceptin control groups.

5.15. The Committee considered that a managed change to biosimilar trastuzumab (Trazimera) would not have any impact on the health benefits or risk associated with reference trastuzumab (Herceptin). The Committee considered that switching between trastuzumab products appears to be safe, despite limited evidence at this time. The Committee also noted that there is no specific evidence of combining pertuzumab with Trazimera at this time, but that other biosimilar studies identify no problems.

Suitability

5.16. The Committee considered that there are no features of Trazimera which would impact on use that would be different from currently funded trastuzumab product (Herceptin).

6. Retreatment with trastuzumab following disease progression in metastatic breast cancer

6.1. The Committee reviewed a paper from Pharmac staff regarding retreatment with trastuzumab following disease progression in metastatic breast cancer.

6.1.1. The Committee noted Pharmac staff had received a request to reconsider widened access to trastuzumab alongside the competitive procurement process for intravenous trastuzumab.

6.2. The Advisory Committee took into account, where applicable, Pharmac's relevant decision-making framework when considering this agenda item.

Recommendation

6.3. The Advisory Committee **recommended** that the application for retreatment with trastuzumab following disease progression be **declined** within the context of treatments of malignancy.

6.4. The Committee noted there was an unmet health need in this setting, in particular for Māori and Pacific peoples with breast cancer. The Committee also noted the competitive procurement process for trastuzumab was expected to improve the net price of trastuzumab. However, the Committee considered that there was no evidence to support the efficacy of trastuzumab in this setting and that trastuzumab would not address the unmet health need.

Māori health impact

6.5. The Committee noted it had considered the impact of HER-2 positive breast cancer on Māori at previous meetings in detail, in particular the high health need and poor health outcomes experienced by Māori with breast cancer.

Discussion

6.6. The Committee noted it considered a funding application for trastuzumab following disease progression in the metastatic setting from the Breast Cancer Special Interest Group in 2010. At the time the Committee considered it was not cost-effective and was an inappropriate use of trastuzumab based on available evidence (CaTSoP meeting November 2010 - record).

6.7. The Committee noted trastuzumab was approved for a range of oncology indications, including for the treatment of patients with metastatic breast cancer who have tumours that overexpress HER2:

- as monotherapy for the treatment of those patients who have received one or more chemotherapy regimens for their metastatic disease; or
- in combination with taxanes for the treatment of those patients who have not received chemotherapy for their metastatic disease; or
- in combination with an aromatase inhibitor for the treatment of post-menopausal patients with hormone-receptor positive metastatic breast cancer (Medsafe datasheet).

6.8. The Committee considered individuals with metastatic breast cancer who experience disease progression are now offered trastuzumab emtansine (TDM-1). The Committee considered there was an unmet health need for people who experience disease progression on treatment with TDM-1, however there was no significant evidence to support the efficacy of trastuzumab following TDM-1 treatment.

6.9. The Committee considered that TDM-1 is well tolerated and that people who were precluded from treatment with TDM-1 (eg due to comorbidities) were unlikely to be suitable candidates for continued chemotherapy in combination with trastuzumab. The response rates of trastuzumab monotherapy in this context were likely to be very poor and the Committee considered there would be insufficient benefit in offering funded trastuzumab as monotherapy for people who were unable to received TDM-1.

6.10. The Committee noted one meta-analysis seeking to assess the safety and effectiveness of retreatment with trastuzumab in HER-2 positive metastatic breast cancer which had been published since its previous consideration in 2010 Han et al; Cancer Manag Res. 2019 May), but prior to the availability of TDM-1. Overall, the

Committee did not consider this meta-analysis provided strong evidence to support the funding of trastuzumab retreatment in our current treatment environment.

6.11. The Committee noted the results of the meta-analysis suggested potential benefits from retreatment following prior trastuzumab, but not TDM-1, and confirmed the safety of retreatment therapy with trastuzumab. However, the Committee considered the meta-analysis to be of poor quality, as the studies included were heterogeneous in design and included a number which did not compare trastuzumab to placebo and others which considered use of the drug in the metastatic setting after prior adjuvant use (where it is already allowed in New Zealand under specified criteria). Given the poor quality of the meta-analysis and its failure to directly address the question of concern the Committee did not consider it appropriate to support the funding of trastuzumab retreatment with the available evidence.

7. Implementation for a possible change to a biosimilar trastuzumab

Discussion

7.1. The Committee reviewed a paper from Pharmac staff regarding the proposed changes to the funding of trastuzumab for people with breast cancer and the associated implementation options to support the change from the trastuzumab reference product (Herceptin) to a biosimilar trastuzumab product, ahead of public consultation.

7.2. The Committee noted both it and PTAC had considered trastuzumab biosimilars multiple times previously, including in:

- August 2019 when PTAC reviewed the clinical evidence for a specific biosimilar trastuzumab product, Herzuma and recommended Pharmac could progress a competitive procurement process for trastuzumab and that a managed change to a single trastuzumab biosimilar product would be clinically acceptable;
- October 2019 when the Cancer Treatments Subcommittee of PTAC (CaTSoP, now CTAC) reviewed the clinical evidence for a specific biosimilar tratsuzumab product, Herzuma and recommended Pharmac could progress a competitive procurement process for trastuzumab and that a managed change to a single trastuzumab biosimilar product would be clinically acceptable. CaTSoP also considered a 6-month transition period would be appropriate;
- July 2020 when CaTSoP members provided advice (via email) on potential commercial and implementation options for a competitive procurement process and:
    - considered patients should not return to the reference trastuzumab (Herceptin) following disease progression
    - indicated a preference that patients should not be transitioned to a different trastuzumab more than once, and that security of supply would be important to enable this
    - considered education of biosimilars would be critical for patients and healthcare professionals in order to alleviate anxiety and reduce the risk of associating disease progression with any change
    - did not identify a group of patients who had clinical circumstances that would prohibit them transitioning to a biosimilar trastuzumab product.
- April 2022 when CTAC provided advice on the potential commercial and implementation options for a trastuzumab competitive procurement process and:
    - supported a competitive process for the supply of trastuzumab, including a 6-month transition period should a change result from the process, in line with previous advice.

- considered a process should be available which enabled people to return to funded Herceptin following a transition from Herceptin to a biosimilar
- considered further assessment of the use of trastuzumab in other indications, particularly gastric cancer, was warranted.

7.3. The Committee noted Pharmac released an RFP seeking proposals for Principal Supply Status (PSS) of intravenous trastuzumab on 8 September 2022.

7.4. The Committee noted the award of Principal Supply Status to a biosimilar trastuzumab would result in a biosimilar being the main funded trastuzumab product in New Zealand. Individuals receiving the currently funded Herceptin brand of trastuzumab would be required to transition, unless their treatment course concluded prior to the end of the transition period.

7.5. The Committee noted the Principal Supplier would be guaranteed at least 95% of the trastuzumab market as the Principal Supplier, with a 5% Alternative Brand Allowance. This would mean the Herceptin brand of trastuzumab would remain funded for use in up to 5% of individuals. The Committee considered it appropriate that the alternative brand allowance would likely be utilised at Pharmac's discretion, and managed via the Exceptions Framework.

7.6. The Committee considered the following Special Authority for trastuzumab for breast cancer would be appropriate, to incorporate its previous recommendations regarding treatment holidays in the metastatic setting (CaTSoP November 2021 meeting record) and Pharmac's Schedule standards:

> **Initial application — (early breast cancer)** ~~only~~ from **any relevant practitioner** ~~a relevant specialist or medical practitioner on the recommendation of a relevant specialist~~. Approvals valid for 15 months for application meeting the following criteria:
> All of the following:
> 1. The patient has early breast cancer expressing HER-2 IHC 3+ or ISH + (including FISH or other current technology): and
> 2. Maximum cumulative dose of 106 mg/kg (12 months' treatment)
> 3. Any of the following
>   - 3.1 9 weeks' concurrent treatment with adjuvant chemotherapy is planned; or
>   - 3.2 12 months' concurrent treatment with adjuvant chemotherapy is planned; or
>   - 3.3 12 months' sequential treatment following adjuvant chemotherapy is planned; or
>   - 3.4 12 months' treatment with neoadjuvant chemotherapy is planned; or
>   - 3.5 Other treatment regimen, in association with adjuvant chemotherapy, is planned.
>
> **Initial application — (metastatic breast cancer)** only from **any relevant practitioner** ~~a relevant specialist or medical practitioner on the recommendation of a relevant specialist~~. Approvals valid for 12 months for application meeting the following criteria:
> All of the following:

1. The patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and
2. Either:
   - 2.1 The patient has not previously received lapatinib treatment for HER-2 positive metastatic breast cancer; or
   - 2.2 Both:
     - 2.2.1 The patient started lapatinib treatment for metastatic breast cancer but discontinued lapatinib within 3 months of starting treatment due to intolerance; and
     - 2.2.2 The cancer did not progress whilst on lapatinib; and
3. Either:
   - 3.1 Trastuzumab will not be given in combination with pertuzumab; or
   - 3.2 All of the following:
     - 3.2.1 Trastuzumab to be administered in combination with pertuzumab; and
     - 3.2.2 Patient has not received prior treatment for their metastatic disease and has had a treatment-free interval of at least 12 months between prior (neo)adjuvant chemotherapy treatment and diagnosis of metastatic breast cancer; and
     - 3.2.3 The patient has good performance status (ECOG grade 0-1); and
4. Trastuzumab not to be given in combination with lapatinib; and
5. Trastuzumab to be discontinued at disease progression.

Renewal — (metastatic breast cancer) only from **any relevant practitioner** ~~a relevant specialist or medical practitioner on the recommendation of a relevant specialist~~. Approvals valid for 12 months for applications meeting the following criteria: ~~All of the following:~~

Either:

1. **All of the following:**
   - 1.1 The patient has metastatic breast cancer expressing HER-2 IHC 3+ or ISH+ (including FISH or other current technology); and
   - 1.2 The cancer has not progressed at any time point during the previous 12 months whilst on trastuzumab; and
   - 1.3 Trastuzumab not to be given in combination with lapatinib; and
   - 1.4 Trastuzumab to be discontinued at disease progression; or
2. **All of the following:**
   - **2.1 Patient has previously discontinued treatment with trastuzumab for reasons other than severe toxicity or disease progression; and**
   - **2.2 Patient has signs of disease progression; and**
   - **2.3 Disease has not progressed during previous treatment with trastuzumab.**

Transition

7.7. The Committee reiterated its previous considerations that a 6-month transition period would be appropriate, as discussed previously. The Committee noted trastuzumab was funded for a maximum of 12 months for early breast cancer. The Committee considered that trastuzumab is now commonly administered for 6 months for early breast cancer (rather than 12). Therefore, many individuals with early breast cancer would not be required to transition, as their treatment with trastuzumab would be completed prior to the end of the transition period.

7.8. The Committee considered most individuals are seen every 12 weeks, and so a 6-month transition would allow adequate time for prescribers to discuss the transition with individuals and that a transition to a biosimilar would not create the need for additional appointments.

7.8.1. The Committee noted that each individual's health journey is unique, and some individuals may be very comfortable with the transition following one appointment, while other individuals may require more time to understand what the transition means for their health journey. The Committee considered early communication with prescribers would allow them to initiate conversations prior to the transition period, to ensure individuals would have adequate time to engage with the available information about the transition.

7.9. The Committee considered early communication and consultation with individuals receiving trastuzumab would support a smooth transition for individuals. The Committee considered a multi-media, multi-pronged approach would be needed, to ensure individuals and healthcare professionals were well supported in understanding and discussing the transition. The Committee considered different modes of communication may be needed in different areas, to reflect the diversity of needs of the local population.

7.10. The Committee considered a single transition for all individuals at once, at each infusion centre would be helpful for clinicians and healthcare teams, limiting the risk of individuals moving back and forth between brands.

7.10.1. The Committee considered pharmacies would need processes in place to manage two brands during the transition period. The Committee considered early communication to the sector would provide time for pharmacies to develop these processes ahead of the transition period.

Alternative brand allowance

7.11. The Committee considered it would be appropriate to retain funded access to Herceptin, as the alternative brand, for individuals who have exceptional clinical circumstances such as a reaction to a trastuzumab biosimilar where they had not previously experienced a reaction to the Herceptin brand.

7.11.1. The Committee did not identify any other populations who may require ongoing funded access to the Herceptin brand, however considered access via the Exceptional Circumstances framework would be appropriate. The Committee considered clear communication on this process for individuals and healthcare professionals as part of a transition would be important.

Implementation support

7.12. The Committee was made aware of evidence (Papautsky & Hamlish. Breast Cancer Res Treat. 2020;184:249-54) that highlighted differences in opinion between individuals and their prescribers about biosimilars. The Committee considered this highlighted the importance of accurate and culturally appropriate information for individuals, to support them in their health journey and alleviate any potential concerns about a biosimilar. The Committee considered advocacy and support groups would play a key role in providing this information, alongside individuals' prescribers and healthcare services.

7.13. The Committee highlighted three key groups to consider as part of the implementation of a biosimilar trastuzumab product: individuals and their whānau, nurses and clinicians who support people with breast cancer, and pharmacies. The Committee considered it important Pharmac engage early with key stakeholders to develop appropriate materials for each group, and noted staff had already started engagement during the process.

7.13.1. The Committee considered the following activities would support individuals and their whānau through a transition to a biosimilar trastuzumab:

- engagement with advocacy and support groups
- engagement with cancer nurse specialists and nurse navigators
- webinars
- electronic and written education
- links to advocacy and support groups and relevant newsletters
- engagement with local kaumatua
- material available in multiple languages.

7.13.2. The Committee considered the following activities would support nurses, clinicians and other healthcare professionals who support people with breast cancer through a transition to a biosimilar trastuzumab:

- webinars and education series regarding biosimilars
- electronic and written education materials
- links to foundations and materials to provide to individuals with breast cancer
- engagement with clinicians, nurses and support teams.

7.13.3. The Committee considered the following activities would support pharmacies through a transition to a biosimilar trastuzumab:

- systems and/or processes to deal with different products (ie the biologic and a biosimilar)
- information regarding extended stability.

7.13.3.1. The Committee highlighted the current capacity issues for infusion services resulted in bulk storage (and therefore stability of compounded medicines) becoming more important for Te Whatu Ora hospitals. The Committee noted Pharmac had included a requirement for extended stability data as part of its competitive procurement process.

7.13.3.2. The Committee noted many hospitals utilise third party compounding providers and considered Pharmac would need to ensure these parties had adequate lead time to ensure ongoing service delivery for a new funded trastuzumab product.

7.13.3.3. The Committee did not consider it needed to review stability data, however considered Pharmac should engage with compounding pharmacists and third party compounding providers ahead of a transition to a biosimilar.