7.12 TRASTUZUMAB DERUXTECAN, Powder for I.V. infusion 100 mg, Enhertu®, ASTRAZENECA PTY LTD.

1 Purpose

1.1 The early re-entry resubmission requested a Section 100 (Efficient Funding of Chemotherapy) listing for trastuzumab deruxtecan (T-DXd) for the treatment of patients with human epidermal growth factor receptor 2 (HER2) low (immunohistochemical [IHC] 1+ or IHC 2+ and in situ hybridisation [ISH] negative) unresectable breast cancer and/or metastatic breast cancer.

1.2 The resubmission was based on the PBAC decision to not recommend T-DXd for this indication at its November 2023 meeting. Table 1 outlines the issues raised by the PBAC in November 2023 and how these issues were addressed in the resubmission.

Table 1: Summary of key matters to be addressed

Matter of concern (paragraph reference to T-DXd minutes, November 2023 PBAC meeting)	Response	Addressed?
Revision of inputs to the economic evaluation		
The ESC advised that a respecified base case would be informative for decision making, incorporating (paragraphs 6.58, 7.9):		
(i) adjusted RDIs for T-DXd and TPC to reflect actual dosing regimens	No change	No
(ii) adjustments to subsequent treatment costs as specified in the evaluation;	No change	No
(iii) removal of vial sharing; fixed EFC fees	As requested[a]	Yes
(iv) application of DB-4 pooled utility estimates for PF and the Lloyd et al utility decrement for PD	As requested	Yes
(v) the use of DB-04 KM data in modelling PFS, OS and TTD	As requested[1]	Yes
(vi) use of independent Weibull parametric functions to extrapolate OS (which results in convergence of curves by approximately 6.5 years);	No change	No
(vii) a 10-year time horizon.	As requested	Yes

Matter of concern (paragraph reference to T-DXd minutes, November 2023 PBAC meeting)	Response	Addressed?
Propose a price reduction to achieve an ICER of $45,000 to < $50,000 per QALY, using the respecified base case model [as specified above] (paragraph 7.10)	EMP reduced from $[redacted] to $[redacted] per vial ([redacted]% reduction). Base case ICER $[redacted][1] in ITT population. The PBAC previously noted the economic model was based on the HR positive cohort of the DB-04 study rather than the ITT population. However, the PBAC considered that, for the purposes of an early re-entry submission, this was acceptable because the HR positive cohort represented 90% of the ITT population. The resubmission presented an economic model using the ITT population.	No
Revision to the financial estimates		
The PBAC noted the alternative approach to estimating the number of patients……., proposed by DUSC, based on CDK4/6 inhibitor…..and the PBAC considered this was a reasonable approach to estimate the likely number of eligible patients (paragraph 7.13).	Financial model uses number of initiating patients on CDK4/6 inhibitors as a starting point. However, a number of other assumptions have been changed.	Partially
The PBAC noted the financial estimates need to be updated to apply (i) the modelled treatment duration based on the respecified economic model and	No change to previous submission.	Unclear
(ii) an RDI of 94% (consistent with the respecified economic model) (paragraph 7.13)	RDI remains 90%, consistent with the economic model in the resubmission	No
Propose an RSA with expenditure caps and a rebate above the caps (paragraph 7.14)	No expenditure cap and rebate proposed. However, the resubmission stated the sponsor is willing to work with the PBAC and Department of Health to determine appropriate terms for listing that share the risk of uncertainty in utilisation and budget impact between the company and the Commonwealth.	No

Source: Summary Table 1, pg 2
EMP = ex-manufacturer price; ICER = incremental cost effectiveness ratio; HR = hormone receptor; ITT = intention to treat; QALY = quality adjusted life year; RDI = relative dose intensity; RSA = risk sharing arrangement
a Different methodology than applied by evaluators for November 2023 submission
The redacted values correspond to the following ranges:
[1] $55,000 to < $75,000

2 Background

2.1 T-DXd was approved by the TGA in January 2023 for the following indication: treatment of adult patients with unresectable or metastatic HER2 low (IHC 1+ or IHC 2+/ISH negative) breast cancer who have received prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy. Patients with hormone receptor positive breast cancer should additionally have received and no longer be considered eligible for endocrine therapy.

2.2 The PICO from the previous submission is presented below with changes in the resubmission noted in strikethrough and italics.

Table 2: Key components of the clinical issue addressed by the resubmission

Component	Description
Population	Patients with HER2 low (IHC 1+ or IHC 2+/ISH-negative) unresectable and/or metastatic BC who have received a prior chemotherapy in the metastatic setting or developed disease recurrence during or within 6 months of completing adjuvant chemotherapy. This includes patients with HR positive/HER2 low BC who have received or are ineligible for endocrine therapy and patients with HR negative/HER2 low BC.
Intervention	Trastuzumab deruxtecan (T-DXd)
Comparator	~~HR positive/HER2 low~~: Physician's choice of chemotherapy (TPC), consisting of capecitabine, eribulin, gemcitabine, paclitaxel and nab-paclitaxel. ~~HR negative/HER2 low: Sacituzumab govitecan (SG)~~
Outcomes	• Overall survival • Progression-free survival • Objective response rate • Duration of response • Time to progression • Quality of life • Safety
Clinical claim	~~In patients with HR positive/HER2 low unresectable or metastatic BC,~~ T-DXd has superior efficacy and a *manageable* ~~different but non-inferior~~ safety profile, compared to TPC. ~~In patients with HR negative/HER2 low unresectable or metastatic BC, T-DXd has non-inferior efficacy and a different but non-inferior safety profile, compared to SG.~~

Source: Table 1, T-DXd minutes with amendments in strikethrough and italics
BC = breast cancer; HER2 = human epidermal growth factor receptor 2; HR = hormone receptor; IHC = immunohistochemical; ISH = in situ hybridisation

3 Requested listing

3.1 The resubmission accepted amendments to the previously considered PBS restriction.

Name, manner of administration, form	Maximum amount (units)	No. of repeats	Dispensed price for maximum amount (DPMA)*	Brand & Manufacturer
Trastuzumab deruxtecan, solution for infusion, 100mg/vial	675 mg	8	Public Hospital: Published [$17,540.04] Effective [$ with SPA] Private hospital: Published [$17,827.65] Effective [$ with SPA]	Enhertu® AstraZeneca Pty Ltd

*Special pricing arrangement to apply

Category / Program: Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals
Prescriber type: Medical Practitioners
Restriction type: Authority Required (telephone/online PBS Authorities system
Administrative Advice: Special pricing arrangements apply
Severity: Unresectable and/or metastatic
Condition: HER2-low breast cancer
Indication: Unresectable and/or metastatic HER2-low breast cancer
Clinical criteria:
Patient must have evidence of human epidermal growth factor receptor 2 (HER2)-low disease as demonstrated by in situ hybridisation (ISH) either in the primary tumour or a metastatic lesion – establish this finding once only with the first PBS prescription
AND
Clinical criteria:
Patient must have received prior chemotherapy in the metastatic setting,
OR
Patient must have developed disease recurrence during or within 6 months of completing adjuvant chemotherapy
AND
Clinical criteria:
Patients with hormone receptor positive disease must have received or be ineligible for endocrine therapy, in the metastatic setting
AND
Clinical criteria:
Patient must have at the time of initiating treatment with this drug, a WHO performance status no higher than 1
AND
Clinical criteria:
The treatment must be the sole PBS-subsidised systemic anti-cancer therapy for this PBS indication.
AND
The treatment must not be prescribed where any of the following is present: (i) left ventricular ejection fraction of less than 50%, (ii) symptomatic heart failure; confirm cardiac function testing for the first PBS-prescription only
Treatment criteria:
Patient must be undergoing initial treatment with this drug – the following are true: (i) this is the first prescription for this drug, (ii) this prescription seeks no more than 3 repeat prescriptions; or
Patient must be undergoing continuing treatment with drug – the following are true: (i) there has been an absence of further disease progression whilst on active treatment with this drug, (ii) this prescription does not seek to re-treat after disease progression, (iii) this prescription seeks no more than 8 repeat prescriptions
Prescribing Instructions: HER2-low is defined as an immunohistochemical [IHC] score of 1+ or an IHC score of 2+ and a negative result on in situ hybridization [ISH]).
Prescribing Instructions: Confirm that the following information is documented/retained in the patient's medical records once only with the first PBS prescription: 1) Evidence of HER2-low status 2) Details of prior drug regimens prescribed for the patient 3) Cardiac function test results
Administrative Advice: Increased maximum amounts can be requested where a patient's weight is greater than 125 kg.
Administrative Advice: No increase in the maximum number of repeats may be authorised.
Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).

3.2 The resubmission requested a special pricing arrangement, with a published ex-manufacturer price the same as the current T-DXd listing in HER2 positive patients ($ per vial). The resubmission requested an effective ex-manufacturer price of $ vial

(compared to $ requested in the November 2023 submission) in HER2 low patients. The pre-PBAC response proposed an ex-manufacturer price of $ per vial (% price reduction).

3.3 The proposed listing does not exclude the possibility of sequential usage of sacituzumab govitecan (SG). The PBAC previously considered that there was insufficient evidence to determine whether or not sequential use is likely to be effective (paragraph 3.8, T-DXd minutes, November 2023 PBAC meeting).

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

4 Consideration of evidence

Sponsor hearing

4.1 There was no hearing for this item.

Consumer comments

4.2 The PBAC noted and welcomed the input from organisations (2) via the Consumer Comments facility on the PBS website. The Breast Cancer Network of Australia (BCNA) strongly supported the PBS listing of T-DXd for patients with HER2 low breast cancer. The BCNA noted the delay in recommending subsidy for this important treatment option has considerable implications for consumers, including the financial burden of funding this treatment privately, reduced equity of access, and prolonged psycho-social distress.

4.3 The Medical Oncology Group of Australia (MOGA) also expressed its strong support for the T-DXd resubmission, categorising it as one of the therapies of "highest priority for PBS listing" on the basis of the DESTINY-Breast 04 (DB-04) trial. The PBAC noted that the MOGA presented a European Society for Medical Oncology Magnitude of Clinical Benefit Scale (ESMO-MCBS) for T-DXd, which was limited to 5 (out of a maximum of 5, where 5 and 4 represent the grades with substantial improvement), based on a comparison with treatment of physician's choice[1].

Comparator

4.4 The previous submission nominated treatment of physician's choice (TPC) (comprising capecitabine, gemcitabine, eribulin, nab-paclitaxel, or paclitaxel) as the main comparator for HR positive/HER2 low patients and SG as the main comparator for HR negative/HER2 low patients. At the November 2023 meeting, the PBAC considered SG was likely to be the preferred treatment in the HR negative population given the available clinical evidence for SG was more robust. The PBAC therefore considered the

[1] Cherny NI, Dafni U, Bogaerts J, et al: ESMO-Magnitude of Clinical Benefit Scale version 1.1. Annals of Oncology 28:2340-2366, 2017

appropriate comparator was TPC for the entire HER2 low population. The resubmission nominated TPC as the comparator for the HER2 low population, noting the HR positive cohort represents approximately 88% of the HER2 low population.

Comparative effectiveness

4.5 No additional clinical evidence was provided in the resubmission.

4.6 The clinical claim for T-DXd in HER2 low patients was based on a single head-to-head randomised controlled trial comparing T-DXd to TPC, known as DB-04. The results for progression free survival (PFS) (median 15.3 months of follow up) and overall survival (OS) (median 32 months of follow up) for the full analysis set (FAS) population is provided in Table 3, Table 4 and Figure 1. Approximately 89% of the trial population were HR positive.

Table 3: Summary of PFS by BICR in DB-04 (DCO 1 January 2022, 15.3 months median follow-up)

PFS by BICR FAS	T-DXd (N=373)	TPC (N=184)	Absolute difference	Hazard ratio (95% CI)
Patients with event (%)	234 (65.1)	127 (69.0)	-	-
Disease progression (%)	208 (55.8)	117 (63.6)	-	-
Death (%)	35 (9.4)	10 (5.4)	-	-
Median PFS months (95% CI)	9.9 (9.0, 11.3)	5.1 (4.2, 6.8)	4.8	**0.50 (0.40, 0.63)**
Proportion of patients alive and progression-free over time				
At 6 months (95% CI)	68.1 (63.0, 72.6)	43.9 (35.9, 51.6)	24.2	-
At 12 months (95% CI)	41.9 (36.6, 47.2)	21.8 (15.3, 29.2)	20.1	-
At 18 months (95% CI)	29.7 (24.4, 35.2)	10.9 (5.7, 18.1)	18.8	-
At 24 months (95% CI)	18.1 (11.9, 25.4)	8.2 (3.2, 16.3)	9.9	-

Source: Table 4, T-DXd minutes, November 2023 PBAC meeting

CI = confidence interval; DB-04 = DESTINY-Breast04; DCO = data cut-off; FAS = full analysis set;; T-DXd = trastuzumab deruxtecan; TPC = treatment of physician's choice.

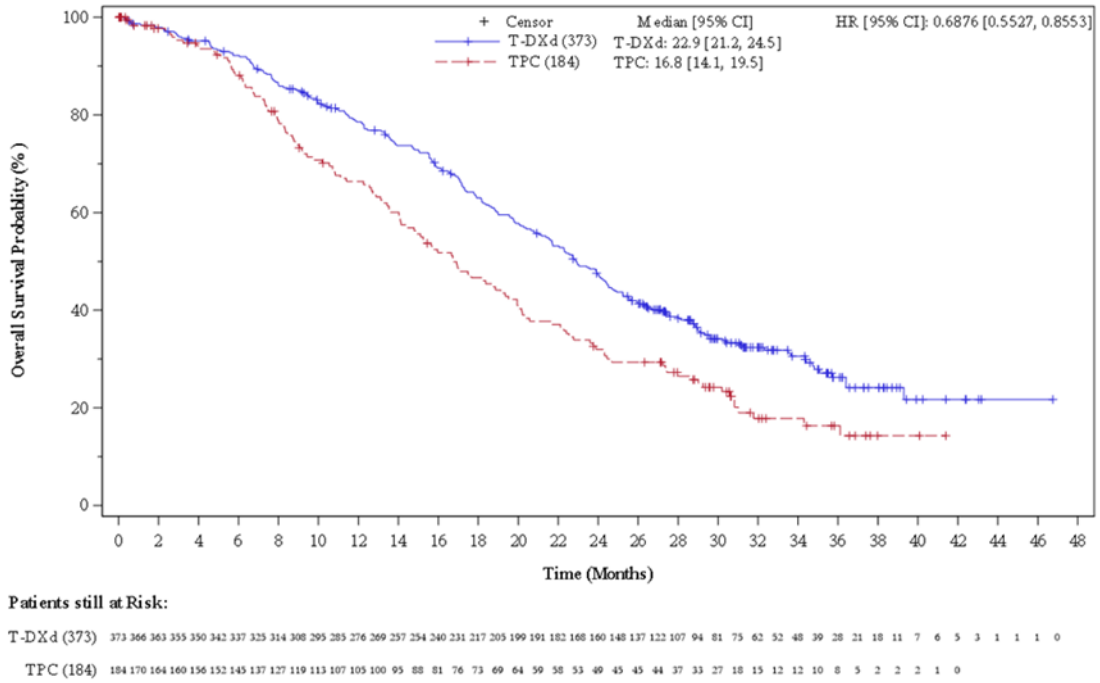
Table 4: Summary of OS in the DB-04 trial (DCO 1 March 2023, 32 months median follow-up)

OS, FAS	T-DXd (N=373)	TPC (N=184)	Absolute difference	Hazard ratio (95% CI)
Patients with event (%)	242 (64.9)	128 (69.6)	-	-
Median OS, months (95% CI)	22.9 (21.5, 24.5)	16.8 (14.1, 19.5)	6.1	**0.69 (0.55, 0.86)**
Proportion of patients alive over time				
At 12 months (95% CI)	78.5 (74.0, 82.4)	66.3 (58.5, 73.0)	12.2	-
At 18 months (95% CI)	63.0 (57.8, 67.8)	46.7 (38.8, 54.2)	16.3	-
At 24 months (95% CI)	47.3 (41.9, 52.4)	32.0 (24.8, 39.3)	15.3	-
At 36 months (95% CI)	26.2 (20.8, 31.9)	16.3 (10.3, 23.6)	9.9	-
At 42 months (95% CI)	21.7, (15.2, 28.9)	NE (NE, NE)	-	-

Source: Table 5, T-DXd minutes, November 2023 PBAC meeting

CI = confidence interval; DB-04 = DESTINY-Breast04; DCO = data cut-off; FAS = full analysis set; HR = hormone receptor; OS = overall survival; T-DXd = trastuzumab deruxtecan; TPC = treatment of physician's choice.

Figure 1: OS for the FAS population in the DB-04 trial (1 March 2023 DCO)



Source: Figure 4, T-DXd minutes, November 2023 PBAC meeting
CI = confidence interval; DCO = data cut-off; FAS = full analysis set; N = number of patients; NE = not estimable; OS = overall survival; T-DXd = trastuzumab deruxtecan; TPC = treatment of physician's choice.

Clinical claim

4.7 The PBAC previously considered that the claim of superior comparative effectiveness, in terms of PFS and OS, was reasonable for the HER2 low population (paragraph 7.7, T-DXd minutes, November 2023 PBAC meeting). However, the PBAC did not accept the submission's claim of non-inferior safety and considered that, overall, T-DXd was of inferior safety compared with TPC, however considered the side effects associated with T-DXd were manageable (paragraph 7.8, T-DXd minutes, November 2023 PBAC meeting).

4.8 The resubmission stated that T-DXd is associated with a manageable safety profile.

Economic analysis

4.9 As an early re-entry resubmission, the economic analysis has not been independently evaluated.

4.10 The previous submission presented a cost-utility analysis based on the outcomes for the HR positive cohort of the DB-04 trial. The PBAC advised the respecified base case model proposed by the ESC (with more conservative assumptions) would form a reasonable basis for a resubmission using the early re-entry pathway. The respecified base case incorporated (i) adjustments to the relative dose intensity (RDI) for T-DXd and TPC to reflect actual dosing regimens; (ii) adjustments to subsequent treatment costs as specified in the evaluation; (iii) removal of vial sharing; (iv) application of DB-04 pooled utility estimates for progression free (PF) health state and the Lloyd et al

utility decrement for the progressive disease (PD) health state; (v) the use of DB-04 KM data in modelling PFS, OS and time to treatment discontinuation (TTD); (vi) use of independent Weibull parametric functions to extrapolate OS (which resulted in convergence of curves by approximately 6.5 years); and (vii) a 10 year time horizon. The ESC noted this resulted in an ICER of $155,000 to < $255,000 per QALY gained (using the price proposed in the November 2023 submission).

4.11 A summary of the economic model parameters in the resubmission and how they compare to the PBAC respecified base case model is provided in Table 5.

Table 5: Summary of economic model parameter changes and updates

November 2023 submission	PBAC respecified base case model	March 2024 resubmission
HR+ population	HR+ population	ITT population
Vial sharing and proportional EFC fees	No vial sharing and fixed EFC fees. Methodology based on distribution around patients' body weight	No vial sharing and fixed EFC fees. Methodology based on average vial usage and rounding up to the nearest vial. The methodology based on distribution around body weight is more appropriate.
90% RDI for T-DXd and CSR RDIs for TPC drugs	RDI equating to mean actual dose / dose in Australian Product Information	No change to November 2023 submission
Subsequent treatment costs: As reported in DB-04 trial	Recalculated among progressed patients	No change to November 2023 submission
OS extrapolation: Log-logistic in both arms	Independent Weibull in both arms	No change to November 2023 submission
Utility values: Treatment specific values as reported in DB-04 trial	Pooled utility values for PF health state and applying Lloyd decrement to PD health state values	Pooled utility values for PF health state and applying Lloyd decrement to PD health state values
Time Horizon: 12 years	10 years	10 years
No KM data used in model	Include KM data for OS, PFS and TTD	Included KM data for OS, PFS and TTD using methodology from Gebski to apply truncation

Source: Table 3.1, resubmission

CSR = clinical study report; EFC = Efficient Funding of Chemotherapy; HR = hormone receptor; ITT = intention to treat; KM = Kaplan Meier; OS = overall survival; PD = progressive disease PFS = progression free survival; RDI = relative dose intensity; TPC = treatment of physician's choice; TTD = time to treatment discontinuation

4.12 A summary of the results of the economic analysis is provided in Table 6. For reference, the modelled results using the base case model from the November 2023 submission and the PBAC respecified model are also included. The pre-PBAC response proposed a vial price of $ which resulted in an ICER of $55,000 to < $75,000 per QALY gained.

Table 6: Results of the economic analysis

	T-DXd	TPC	Increment
March 2024 resubmission (ITT population, $ EMP per vial)			
Costs	$	$54,541	$
QALYs	1.84	1.31	0.53
Incremental cost/extra QALY gained			**$**[1]
Pre-PBAC response (ITT population, $ EMP per vial)			
Costs	$	$54,541	$
QALYs	1.84	1.31	0.53
Incremental cost/extra QALY gained			**$**[1]
November 2023 submission (HR+ population, EMP $ per vial)			
Costs	$	$53,892	$
QALYs	2.17	1.63	0.54
Incremental cost/extra QALY gained			**$**[2]
PBAC respecified model (HR+ population, EMP $ per vial)			
Costs	$	$52,748	$
QALYs	1.641	1.230	0.411
Incremental cost/extra QALY gained			**$**[3]

Source: Table 3.5, resubmission; Table 12, T-DXd minutes, November 2023 PBAC meeting

EMP = ex-manufacturer price; HR = hormone receptor; ITT = intention to treat; QALY = quality adjusted life year; T-DXd = trastuzumab deruxtecan; TPC = treatment of physician's choice.

The redacted values correspond to the following ranges:

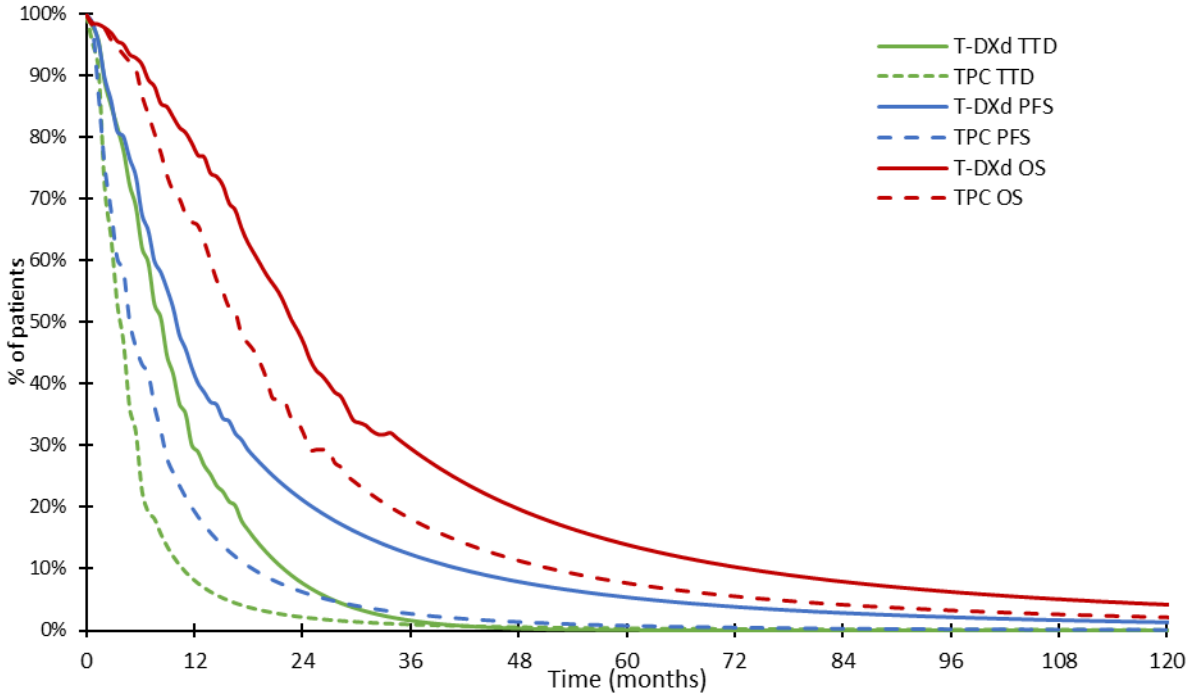
[1] *$55,000 to < $75,000*

[2] *$75,000 to < $95,000*

[3] *$155,000 to < $255,000*

4.13 The model traces for TTD, PFS and OS over the time horizon of the model are provided in Figure 2. The PBAC noted the modelled OS curve resulted in approximately 4% of people remaining alive at 10 years in the T-DXd arm using the log logistic function and 0% using the Weibull function.

Figure 2: Model traces



Source: Section 3 spreadsheet provided with resubmission
OS = overall survival; PFS = progression free survival; T-DXd = trastuzumab deruxtecan; TPC = treatment of physician's choice; TTD = time to treatment discontinuation;

4.14 The PBAC previously considered that a base case ICER of $45,000 to $50,000 per QALY would be appropriate in the HER2 low population, based on previous considerations in similar patient populations (i.e., eribulin, CDK4/6 inhibitors) and the moderate clinical need. The PBAC recalled it had recommended pembrolizumab and SG for triple negative breast cancer (TNBC) with higher ICERs but noted TNBC was an aggressive condition, with poorer survival and fewer treatment options. The PBAC also recalled it had recommended T-DXd for HER2 positive breast cancer with a higher ICER but noted this was also an aggressive condition and the relative benefit of treatment was substantially higher (paragraph 7.10, T-DXd minutes, November 2023 PBAC meeting). The resubmission stated that it would be a significant challenge to accept all the PBAC specified conditions, especially at the ICER range of $45,000 to $50,000 per QALY whilst appropriately representing the value of T-DXd in this indication. The resubmission stated that the inclusion of the HR negative (i.e., TNBC) population in the economic model justified an ICER threshold closer to $75,000 to < $95,000 per QALY.

4.15 The resubmission stated that patients with HER2 low HR positive disease have poor survival outcomes after initial systemic treatment (median overall survival of ~ 18 months) (Modi, et al 2022). Patients with HER2 low HR negative disease, have even worse survival outcomes following second to third line chemotherapy (median overall survival of ~ 8 months in exploratory analysis) (Modi, et al, 2022) as survival outcomes decline steeply on subsequent chemotherapy and patients have limited alternatives.

The resubmission noted the PBAC previously considered that SG would be the preferred treatment in the HR negative population suggesting sequential use of SG and T-DXd (paragraph 3.8, 4.5, T-DXD minutes, November 2023 PBAC meeting) thus positioning T-DXd in TNBC in a higher clinical need population (i.e., later line treatment). The resubmission stated that following this logic would warrant a higher ICER in a patient group of high unmet clinical need with limited treatment options.

4.16 Key sensitivity analyses are presented in Table 7.

Table 7: Key sensitivity analyses

Analyses	Incremental cost ($)	Incremental QALY	ICER	Change
Base case	[redacted]	0.532	[redacted][1]	-
Population (base case ITT population) • HR+ population (**#5**)	[redacted]	0.474	[redacted][2]	+[redacted]%
Parametric function for OS extrapolation (base case log logistic for T-DXd and TPC)				
• Weibull for T-DXd and TPC (**#4**)	[redacted]	0.458	[redacted][2]	+[redacted]%
Adjusted RDIs for T-DXd and TPC to reflect actual dosing regimens (**#1**)		0.532	[redacted][2]	+[redacted]%
Adjusted subsequent treatment costs as specified in the previous evaluation (**#2**)		0.532	[redacted][2]	+[redacted]%
Adjustment to calculating EFC fees as specified in previous evaluation (**#3**)		0.532	[redacted][2]	+[redacted]%
Multi-variate				
#1 + #2 + #3	[redacted]	0.532	[redacted][2]	+[redacted]%
#1 + #2 + #3 using the price in the pre-PBAC response[1]		0.532	[redacted][2]	+[redacted]%
#1 + #2 + #3 + #4		0.468	[redacted][3]	+[redacted]%
#1 + #2 + #3 + #4 using the price in the pre-PBAC response[1]		0.458	[redacted][2]	+[redacted]%
#1 + #2 + #3 + #4 + #5		0.413	[redacted][4]	+[redacted]%
#1 + #2 + #3 + #4 + #5 using the price in the pre-PBAC response[1]		0.413	[redacted][3]	+[redacted]%

Source: Section 3 spreadsheet provided with resubmission

EFC = Efficient Funding of Chemotherapy; EMP = ex-manufacturer price; HR+ = hormone receptor positive; ITT = intention to treat; RDI = relative dose intensity; TPC = treatment of physicians choice.

1. EMP $[redacted] per vial

The redacted values correspond to the following ranges:

[1] *$55,000 to < $75,000*

[2] *$75,000 to < $95,000*

[3] *$95,000 to < $115,000*

[4] *$115,000 to < $135,000*

4.17 In November 2023, the PBAC noted the economic model was based on the HR positive cohort of the DB-04 study rather than the ITT population. However, the PBAC considered that, for the purposes of an early re-entry submission, this was acceptable because the HR positive cohort represented 90% of the ITT population (paragraph 7.11, T-DXd minutes, November 2023 PBAC meeting). The resubmission considered the ITT population is the most appropriate data set given the PBAC advice to not separately model the HR negative patients. This is inconsistent with the early re-entry pathway advice from PBAC and complicates validating the model included in the resubmission versus the model evaluated as part of the November 2023 submission

(which was for the HR positive population). Limiting the model provided in the resubmission to the HR positive population increased the ICER from $55,000 to < $75,000 to $75,000 to < $95,000 per QALY gained. The PBAC previously considered SG was likely to be the preferred treatment option for the HR negative population (paragraph 7.6, T-DXd minutes, November 2023 PBAC meeting) so the extent of use in the HR negative population is potentially small.

4.18 In the previous economic model, TTD, PFS and OS curves were modelled over the entire time horizon using parametric functions and consequently no KM data was explicitly included in the model. Additionally, as there was no application of treatment waning to the parametric functions, the modelled curves represented an ongoing treatment effect of T-DXd, in terms of OS, until the end of the time horizon, which was not justified. The PBAC respecified base case model incorporated the use of KM data in modelling PFS, OS and TTD and applied an independent Weibull curve for OS which had better visual and statistical fit than the submission's base case and resulted in convergence of the OS curves at approximately 6.5 years. The resubmission used KM data (with truncation points determined using methodology reported in Gebski 2018) but maintained the use of a log-logistic parametric function. Using a Weibull parametric extrapolation for OS curves (but maintaining the resubmission's approach to determining truncation point for PFS, OS and TTD) resulted in an ICER of $75,000 to < $95,000 per QALY gained.

4.19 The pre-PBAC response noted the Weibull AFT extrapolation predicted 5-year survival rates for T-DXd and TPC of 5% and 2%, respectively. The pre-PBAC response noted the log-logistic extrapolation proposed in the resubmission predicts rates of 14% and 8% for T-DXd and TPC, respectively, which it considered are much more realistic 5-year survival rates for HER2 low population.

4.20 The PBAC respecified economic model incorporated a number of changes related to vial sharing and the use of proportional EFC fees, changes to the RDI for T-DXd and TPC and how subsequent treatments were accounted for. The resubmission either did not fully accept these changes or applied a different methodology than used in the previous evaluation. Implementing these changes as recommended by the PBAC increased the ICER to $75,000 to < $95,000 per QALY gained.

4.21 A multi-variate analysis incorporating all the changes outlined in paragraphs 4.18, 4.19 and 4.21 resulted in an ICER $115,000 to < $135,000 per QALY (using the price proposed in the resubmission). Using the price proposed in the November 2023 submission resulted in an ICER of $135,000 to < $155,000 which does not match the ICER in the previous minutes ($155,000 to < $255,000, paragraph 7.9, T-DXd minutes, November 2023 PBAC meeting). Some of the difference is likely due to different truncation points being used for extrapolation of PFS, OS and TTD.

Drug cost per patient per course

4.22 Using the price proposed in the resubmission, the modelled T-DXd cost per patient was $ (undiscounted), based on average treatment duration of 10.49 months. The

financial estimates applied a different treatment duration for HR positive (10.96 months) and HR negative (7.65 months) for a cost per patient of $ and $, respectively.

Table 8: Drug costs per patient per course for T-DXd (using the price proposed in the resubmission

	Economic Model	Financial Estimates
Mean duration (months)	10.49 months	10.96 months for HR positive 7.65 months for HR negative
Cost/patient/cycle	$	$
Cost/patient/course	$	$ for HR positive (approximately 70% of treated patients over 6 years) $ for HR negative (approximately 30% of treated patients over 6 years)

Source: calculated Section 3 and Section 4 spreadsheets provided with resubmission
HR = hormone receptor; T-DXd = trastuzumab deruxtecan
1. Assuming 90% RDI
2. Calculated as 90% x $. However, 90% is applied to script numbers (as compliance) in the financial model.

Estimated PBS usage and financial implications

4.23 As an early re-entry resubmission, the estimated usage and financial estimates have not been independently evaluated.

4.24 The previous submission utilised an epidemiological approach to estimate the extent of use of T-DXd and the financial impact of listing on the PBS in the HER2 low population. However, the PBAC considered that there was a high level of uncertainty with a number of the assumptions driving the estimated patient numbers (paragraph 7.12, T-DXd minutes, November 2023 PBAC meeting). The PBAC noted the alternative approach to estimating the number of patients with HR positive/HER2 low unresectable or metastatic breast cancer, proposed by DUSC, based on CDK4/6 inhibitor data and the PBAC considered this was a reasonable approach to estimate the likely number of eligible patients (paragraph 7.13, T-DXd minutes, November 2023 PBAC meeting). The PBAC advised an early re-entry pathway resubmission should revise the financial estimates using the alternative approach proposed by DUSC.

4.25 Key changes to the estimated use and financial implications are provided in Table 9.

Table 9: Key changed to inputs for utilisation and financial estimates

Assumption	DUSC assumption	March 2024	Comment
HR positive/HER2 low patients			
Number of patients with HR+/ HR- disease	Incident count of CDK4/6 inhibitor patients	Consistent with DUSC estimates	-
Annual growth in CDK 4/6 inhibitor patients	2%	3.5%	The pre-PBAC response accepted a growth rate of 2%. See paragraph 4.27.
Proportion of HER2low in HR+ patients	61%	68.4%	The pre-PBAC response proposed 65.4%. See paragraph 4.28.
Proportion suitable for T-DXd	80%	Consistent with DUSC estimates	-
Uptake	% in Year 1 % in Years 2-3 and % from Year 4-6	Consistent with DUSC estimates	-

Assumption	DUSC assumption	March 2024	Comment
Treatment duration	10.96 months	Unchanged from previous submission	The PBAC previously advised the financial estimates would need to be updated to apply…the modelled treatment duration based on the respecified economic model. Treatment duration largely consistent with economic model.
Rapid progressors	50 patients per year	Consistent with DUSC estimates	-
Prevalent 3+ pool	621 patients in Year 1 and Year 2	Consistent with DUSC estimates	Calculated using a 5-year exponential curve survival rate of 34%. This results in an estimated 2-year survival rate of 65% (paragraph 6.66, T-DXd minutes, November 2023 PBAC meeting).
HR negative/HER2 low patients			
Incident population with breast cancer	Based on linear projection of AIHW incidence	Consistent with DUSC; however different methodology for projection.	AIHW all age-specific incidence rate data with growth based on linear regression, applied to the ABS population. The DUSC previously considered that it would be more appropriate to use the number of incident breast cancer cases per year and apply a linear projection to the number of incident cases. The resubmission stated this methodology only provided projections for the growing incident cases of breast cancer but does not consider the growing Australian population.
TNBC	15%	Consistent with DUSC estimates	-
Proportion with uBC/mBC	54.8%	Consistent with DUSC estimates	-
Proportion of HER2low in HR- patients	36.6%	48.3%	The pre-PBAC response proposed 36.6%. See paragraph 4.29
Proportion of patients for whom T-DXd is clinically appropriate	50%	65%	The pre-PBAC response proposed 50%. See paragraph 4.30.
Uptake	[redacted]% in Year 1 [redacted]% in Years 2-3 and [redacted]% from Year 4-6	Consistent with DUSC estimates	The PBAC previously advised SG was likely to be the preferred treatment option in HR negative patients (paragraph 7.6, T-DXd minutes, November 2023 PBAC meeting).
Treatment duration	7.65 months	Unchanged from previous submission	Unclear if the treatment duration applied in the financials is consistent with the economic model

4.26 The resubmission applied an annual growth of 3.5% to the number of CDK4/6 patients. The increase in growth from 2% (as proposed by DUSC) to 3.5% was not well supported in the resubmission. The methodology used in the resubmission to estimate the growth in the number of incident patients relied on PBS services which does not

differentiate initial and continuing patients. The patient numbers in the pre-PBAC response were based on applying a growth of 2%.

4.27 The DUSC previously considered the proportion of HR positive patients who are HER2 low was overestimated (80.27%, based on Shang 2023). The DUSC noted the recently published study by Viale 2023 captured the Australian population and estimated the proportion as 63.6%. The DUSC noted other estimates from Schettini 2021 (65.4%) and TROPiCs-02 (56.6%) and considered Shang 2023 may be an outlier. Overall, the DUSC considered 61% would be a more appropriate assumption. The resubmission stated that Shang 2023 should be taken into account and has applied the midpoint of the Shang 2023 and TROPiCs-02 estimate (68.4%). The pre-PBAC response noted the DUSC considered Schettini 2021 was a reasonable source to use for the HR negative population (see paragraph below) and proposed using the proportion from Schettini 2021 for the HR positive population (65.4%).

4.28 The DUSC previously considered that Shang 2023 was also likely to overestimate the proportion of HR negative patients who are HER2 low (60%). The DUSC considered the percentage from Schettini 2021 (36.6%) which used larger patient numbers and is more in line with other literature of smaller studies should be considered as an appropriate alternative. The resubmission stated that Shang 2023 should be taken into account and has applied the midpoint of the Shang 2023 and Schettini 2021 estimate (48.3%). The pre-PBAC response proposed applying 36.6% as reported by Schettini 2021 and as supported by DUSC.

4.29 The DUSC previously considered it would be reasonable to assume 50% of HER2 low/ HR negative patients would be clinically appropriate for T-DXd as accepted for SG. The resubmission stated it is likely T-DXd is a more suitable treatment for a wider patient pool than SG and maintained that 65% would be clinically appropriate. The pre-PBAC response agreed with the DUSC proposed assumption of 50%.

4.30 The estimated number of patients that would initiate treatment with T-DXd is presented in Table 10.

Table 10: HER2-low estimated patient use for T-DXd (as presented in the submission)

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
HR+/HER2-low estimated patient use for T-DXd						
Incident count of CDK4/6 inhibitor patients (3.5% annual growth)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Proportion of HER2 low in HR+ patients (65.4%)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Proportion suitable for T-DXd (80%)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Prevalent pool at 3L+	[redacted][1]	[redacted][1]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Rapid progressors on adjuvant therapy	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Uptake	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Total HR+/HER2low patients	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
HR-/HER2-low estimated patient use for T-DXd						
Incident population based on linear projection of AIHW incidence	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]	[redacted][3]
TNBC in Australia (15%)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Proportion with uBC/mBC (54.8%)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Proportion of HER2 low in HR- patients (48.3%)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Proportion of patients for whom T-DXd is clinically appropriate (65%)	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
Uptake	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%	[redacted]%
Total HR-/HER2low Patients	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]

Source: Table 4.2.1, Table 4.3.1 of resubmission

HR = hormone receptor; mBC = metastatic breast cancer; T-DXd = trastuzumab deruxtecan; TNBC = triple negative breast cancer; uBC = unresectable breast cancer

The redacted values correspond to the following ranges:

[1] *500 to < 5,000*

[2] *< 500*

[3] *20,000 to < 30,000*

4.31 The estimated use and financial implication of listing T-DXd is summarised in Table 11.

Table 11: Estimated financial implications of listing T-DXd

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
March 2024 resubmission						
Number of patients treated	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
HR positive/HER2 low	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
HR negative/HER2 low	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
November 2023 submission						
Number of patients treated	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
HR positive/HER2 low	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
HR negative/HER2 low	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
November 2023 DUSC revised estimates						
Number of patients treated	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
HR positive/HER2 low	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
HR negative/HER2 low	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
March 2024 resubmission						
Number of scripts dispensed	[redacted][3]	[redacted][3]	[redacted][4]	[redacted][4]	[redacted][4]	[redacted][4]
Estimated financial implications of T-DXd						
Cost to PBS/RPBS less co-payments	[redacted][5]	[redacted][5]	[redacted][6]	[redacted][7]	[redacted][7]	[redacted][7]
Estimated financial implications for TPC						
Cost to PBS/RPBS less co-payments	[redacted][8]	[redacted][8]	[redacted][8]	[redacted][8]	[redacted][8]	[redacted][8]
Net financial implications						
March 2024 resubmission						
Net cost to PBS/RPBS	[redacted][5]	[redacted][5]	[redacted][10]	[redacted][6]	[redacted][6]	[redacted][6]
Net cost to MBS	[redacted][9]	[redacted][9]	[redacted][9]	[redacted][9]	[redacted][9]	[redacted][9]
Net cost to PBS/RPBS/MBS	[redacted][5]	[redacted][5]	[redacted][10]	[redacted][6]	[redacted][6]	[redacted][6]
November 2023 submission						
Net cost PBS/RPBS	[redacted][11]	[redacted][11]	[redacted][11]	[redacted][11]	[redacted][11]	[redacted][11]
November 2023 DUSC revised estimates						
Net cost PBS/RPBS	[redacted][5]	[redacted][5]	[redacted][10]	[redacted][10]	[redacted][10]	[redacted][10]

Source: Table 4.2.1, Table 4.3.1, Table 4.4.2 of resubmission; Table 15, Table 16, T-DXd minutes, November 2023 PBAC meeting.

The redacted values correspond to the following ranges:

[1] *500 to < 5,000*

[2] *< 500*

[3] *30,000 to < 40,000*

[4] *20,000 to < 30,000*

[5] *$100 million to < $200 million*

[6] *$80 million to < $90 million*

[7] *$90 million to < $100 million*

[8] *Net cost saving*

[9] *$0 to < $10 million*

[10] *$70 million to < $80 million*

[11] *$200 million to < $300 million*

4.32 The total net cost to the PBS/RPBS of listing T-DXd in the resubmission was estimated to be $100 million to < $200 million in Year 1 with a total cost across the first 6 years of listing of $500 million to < $600 million.

4.33 The total net cost to the PBS/RPBS of listing T-DXd using the number of patients treated provided in the pre-PBAC response and an EMP of $[redacted] per vial was estimated to

be $80 million to < $90 million in Year 1 with a total cost across the first 6 years of listing of $400 million to < $500 million (Table 12).

Table 12: Estimated financial implications of listing T-DXd using treated patients estimates provided in pre-PBAC response

	Year 1	Year 2	Year 3	Year 4	Year 5	Year 6
Estimated extent of use						
Number of patients treated	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
HR positive/HER2 low	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]	[redacted][1]
HR negative/HER2 low	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]	[redacted][2]
Estimated financial implications of T-DXd (EMP of $[redacted] per vial)						
Cost to PBS/RPBS less co-payments	[redacted][3]	[redacted][4]	[redacted][5]	[redacted][5]	[redacted][5]	[redacted][6]

Source: Table 1 of pre-PBAC response with costs calculated using the Section 4 spreadsheet provided with the resubmission
HR = hormone receptor; T-DXd = trastuzumab deruxtecan
The redacted values correspond to the following ranges:
[1] *500 to < 5,000*
[2] *< 500*
[3] *$80 million to < $90 million*
[4] *$90 million to < $100 million*
[5] *$60 million to < $70 million*
[6] *$70 million to < $80 million*

Financial Management – risk sharing arrangement

4.34 The PBAC previously noted the significant cost of listing T-DXd for this population and considered a Risk Sharing Arrangement (RSA) with expenditure caps with a rebate above the caps would be required to address the uncertainty in the patient numbers. To facilitate timely access of T-DXd in patients with HER-2 low, the pre-PBAC response proposed an RSA with expenditure caps and a [redacted]% rebate beyond the caps.

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

5 PBAC Outcome

5.1 The PBAC recommended the Section 100 (Efficient Funding of Chemotherapy) listing of trastuzumab deruxtecan (T-DXd) for the treatment of patients with human epidermal growth factor receptor 2 (HER2) low unresectable or metastatic breast cancer. The PBAC reiterated its previous consideration that T-DXd was superior to chemotherapy and there was a moderate clinical need for additional treatments in this therapeutic area. The PBAC considered the incremental cost effectiveness ratio remained high at the price proposed in the pre-PBAC response and a further reduction in treatment cost would be required. The PBAC considered the estimated number of treated patients provided in the pre-PBAC response was reasonable. The PBAC noted the very high financial cost and risk to the Commonwealth and advised a risk share arrangement with a [redacted]% rebate beyond the financial estimates would be appropriate.

5.2 The PBAC noted the consumer comments received from the Breast Cancer Network of Australia and the Medical Oncology Group of Australia, and also recalled the consumer comments received for its November 2023 consideration.

5.3 The PBAC reiterated its previous consideration there was a moderate clinical need for additional treatments for patients with HER2 low breast cancer (paragraph 7.4, T-DXd minutes, November 2023 PBAC meeting).

5.4 The PBAC advised the restriction criteria provided in the resubmission were appropriate with the following amendment:

- The clinical criterion "Patient must have evidence of human epidermal growth factor receptor 2 (HER2)-low disease ~~as demonstrated by in situ hybridisation (ISH) either in the primary tumour or a metastatic lesion – establish this finding once only with the first PBS prescription~~" could be amended as indicated with strikethrough as this information is covered by the prescribing instruction defining HER2 low.

5.5 The PBAC noted the proposed restriction criteria does not exclude sequential use of T-DXd and sacituzumab govitecan (SG), but considered that the extent of sequential use in the HR negative population was likely to be low and no changes to the criteria were needed.

5.6 The PBAC noted the resubmission proposed treatment of physician's choice (TPC) (comprising capecitabine, gemcitabine, eribulin, nab-paclitaxel, or paclitaxel) as the comparator for the HER2 low population and reiterated its previous consideration that this was the appropriate comparator (paragraph 7.6, T-DXd minutes, November 2023 PBAC meeting).

5.7 The PBAC recalled it had previously considered that the claim T-DXd is superior to TPC in terms of effectiveness in the HER2 low population was reasonable based on the progression free survival (PFS) and overall survival (OS) outcomes from the DB-04 trial (paragraph 4.7). The PBAC recalled that it had also previously considered T-DXd was of inferior safety compared with TPC, but had a manageable safety profile (paragraph 4.7). The PBAC noted no additional clinical data was provided in the resubmission.

5.8 The PBAC noted the resubmission provided a revised economic model that resulted in an ICER of $55,000 to < $75,000 per QALY using the price proposed in the pre-PBAC response (ex-manufacturer price of $ per vial). The PBAC noted the revised economic model included some but not all of the changes requested by PBAC in its November 2023 consideration as discussed below.

5.9 The PBAC noted the revised economic model removed vial sharing, used fixed EFC fees, included revised utility values, proposed a shorter time horizon and incorporated the Kaplan Meier (KM) data from the DB-04 trial, as requested by the PBAC (see Table 5). The PBAC noted the methodology for implementing some of these changes (i.e., fixed EFC fees, point of truncation for the KM data) was different to how the previous evaluation implemented them.

5.10 The PBAC noted the revised economic model did not change the approach to applying relative dose intensity (RDI) and calculating subsequent treatment costs in both treatment arms. The PBAC noted the ICER implementing these changes as requested

previously and using the appropriate methodology for applying fixed EFC fees increased the ICER to $75,000 to < $95,000 per QALY gained using the price proposed in the pre-PBAC response.

5.11 The PBAC noted the revised economic model included patients with HR negative and HR positive HER2 low disease, rather than just HR positive HER2 low disease as requested previously (paragraph 7.11, T-DXd minutes, November 2023 PBAC meeting). However, the PBAC considered this change was reasonable in the context of the clinical claim and the requested PBS listing being in the overall HER2 low population.

5.12 The PBAC noted the revised economic model maintained the log logistic function to extrapolate OS, rather than the Weibull function as requested in November 2023. The PBAC acknowledged the Weibull function may be conservative but considered it remained uncertain whether an ongoing treatment effect of T-DXd for the time horizon of the economic model (i.e., no convergence of OS curves with 4% of patients treated with T-DXd alive at 10 years) was reasonable.

5.13 The PBAC considered it was reasonable to accept the revised economic model which resulted in an ICER of $55,000 to < $75,000 per QALY gained, but noted there were some outstanding uncertainties, as outlined above, relative to the economic model specified by the PBAC in November 2023.

5.14 The PBAC considered that, as previously advised (see paragraph 4.14), T-DXd would be cost-effective with an ICER of $45,000 to $50,000 per QALY gained. The PBAC noted the arguments (as discussed in paragraph 4.15) that inclusion of the HR negative population should allow for a higher ICER but considered an ICER of less than $50,000 QALY gained remained appropriate for T-DXd for the following reasons:

- the extent of use in the HR negative population is uncertain, given the likely preferential use of SG in this population, and the magnitude of clinical benefit of sequential use is also uncertain; and
- there were some outstanding uncertainties associated with the revised economic model. The PBAC noted the ICER may plausibly increase to $75,000 to < $95,000 per QALY gained (see paragraph 5.10) and potentially to $75,000 to < $95,000 per QALY gained if a conservative extrapolation function (i.e., Weibull) is also applied to OS.

5.15 The PBAC considered the estimated number of patients eligible for treatment with T-DXd as proposed in the pre-PBAC response (see Table 12) formed a reasonable basis to estimate the financial implications of listing T-DXd on the PBS. The PBAC noted the financial estimates will need to be updated to reflect the reduced cost of T-DXd.

5.16 The PBAC advised a risk sharing arrangement with expenditure caps and a [redacted]% rebate for any spend over the caps would be required to manage the significant cost of listing T-DXd.

5.17 The PBAC previously advised that T-DXd is not suitable for prescribing by nurse practitioners (paragraph 20.7, T-DXd Public Summary Document (PSD), July 2023 PBAC meeting).

5.18 The PBAC found that the criteria prescribed by the *National Health (Pharmaceuticals and Vaccines – Cost Recovery) Regulations 2022* for Pricing Pathway A were not met. Specifically, the PBAC found that in the circumstances of its recommendation for T-DXd:

a) The treatment is expected to provide a substantial and clinically relevant improvement in efficacy, over alternative therapies, on the basis of the PFS and OS results of the DB-04 study;

b) The treatment is not expected to address a high and urgent unmet clinical need due to the availability of other treatment options;

c) It was not necessary to make a finding in relation to whether it would be in the public interest for the subsequent pricing application to be progressed under Pricing Pathway A because one or more of the preceding tests had failed.

5.19 The PBAC advised that this resubmission would not meet the criteria for an Independent Review as received a positive PBAC recommendation.

Outcome:
Recommended

6 Recommended listing

6.1 Add new item:

MEDICINAL PRODUCT Form		**PBS item code**	**Max. Amount**	**№.of Rpts**
TRASTUZUMAB DERUXTECAN Injection		NEW (Public) NEW (Private)	675 mg	8
Available brands				
Enhertu trastuzumab deruxtecan 100 mg injection, 1 vial				
Restriction Summary [new] / Treatment of Concept: [new]				
Concept ID	**Category / Program:** Section 100 – Efficient Funding of Chemotherapy Public/Private hospitals			
	Prescriber type: ☒Medical Practitioners			
	Restriction type: ☒Authority Required (telephone/online PBS Authorities system)			
	Administrative Advice: Increased maximum amounts can be requested where a patient's weight is greater than 125 kg.			
	Administrative Advice: No increase in the maximum number of repeats may be authorised.			
	Administrative Advice: Special pricing arrangements apply			

	Administrative Advice: Applications for authorisation under this restriction may be made in real time using the Online PBS Authorities system (see www.servicesaustralia.gov.au/HPOS) or by telephone by contacting Services Australia on 1800 700 270 (hours of operation 8 a.m. to 5 p.m. Monday to Friday).
	Severity: Unresectable and/or metastatic
	Condition: HER2-low breast cancer
	Indication: Unresectable and/or metastatic HER2-low breast cancer
	Clinical criteria:
	Patient must have evidence of human epidermal growth factor receptor 2 (HER2)-low disease
	AND
	Clinical criteria:
	Patient must have received prior chemotherapy in the metastatic setting,
	OR
	Patient must have developed disease recurrence during or within 6 months of completing adjuvant chemotherapy
	AND
	Clinical criteria:
	Patients with hormone receptor positive disease must have received or be ineligible for endocrine therapy, in the metastatic setting
	AND
	Clinical criteria:
	Patient must have at the time of initiating treatment with this drug, a WHO performance status ~~a World~~ no higher than 1
	AND
	Clinical criteria:
	The treatment must be the sole PBS-subsidised systemic anti-cancer therapy for this PBS indication.
	AND
	Clinical criteria:
	The treatment must not be prescribed where any of the following is present: (i) left ventricular ejection fraction of less than 50%, (ii) symptomatic heart failure; confirm cardiac function testing for the first PBS-prescription only
	Treatment criteria:
	Patient must be undergoing initial treatment with this drug – the following are true: (i) this is the first prescription for this drug, (ii) this prescription seeks no more than 3 repeat prescriptions; or
	Patient must be undergoing continuing treatment with drug – the following are true: (i) there has been an absence of further disease progression whilst on active treatment with this drug, (ii) this prescription does not seek to re-treat after disease progression, (iii) this prescription seeks no more than 8 repeat prescriptions
	Prescribing Instructions: HER2-low is defined as an immunohistochemical [IHC] score of 1+ or an IHC score of 2+ and a negative result on in situ hybridization [ISH]).
	Prescribing Instructions: Confirm that the following information is documented/retained in the patient's medical records once only with the first PBS prescription: 1) Evidence of HER2-low status 2) Details of prior drug regimens prescribed for the patient 3) Cardiac function test results

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.